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General Comment

Please find Wyoming Mining Association comments on Incorporation of Risk Management Concepts in Regulatory Programs. Part 1,2,3

Attachments

Part_2

Part_1

Part_3

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January 3, 2012

Ms. Cindy Bladey,
Chief, Rules, Announcements, and Directives Branch (RADB)
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Mail Stop: TWB–05–B01M
U.S. Nuclear Regulatory Commission
Washington, DC 20555–0001

Subject: Wyoming Mining Association (WMA) Comments on the Incorporation of Risk Management Concepts in Regulatory Programs Docket ID: NRC–2011– 0269– (Federal Register/Volume. 76, Number. 225 / Tuesday, November 22, 2011 /Notices)

Dear Ms. Bladey:

The Wyoming Mining Association (WMA) is an industry association representing mining companies, contractors, vendors, suppliers and consultants in the State of Wyoming. Among its mining industry members are uranium recovery licensees, including two (2) operating in-situ uranium recovery licensees, one conventional uranium recovery operator in standby, several companies planning new uranium recovery operations that are currently in the permitting process and several companies conducting final reclamation/restoration operations.

The following are the WMA's comments on the ***Incorporation of Risk Management Concepts in Regulatory Programs***:

The WMA strongly supports the incorporation of risk management principles and concepts into all regulatory programs and especially for the portions of the programs addressing uranium recovery for the following reasons:

Inherent Low Risks Involved in Handling of Radioactive Materials in General

The primary risks from radiation from licensed activities are stochastic effects (cancer). Regardless of public perception, the proper handling of radioactive materials pose low risks to workers and to society when compared to other risks (tobacco use, alcohol use, operation of a motor vehicle, slips and falls in the home etc.) that members of society expose themselves to (generally by choice) each day.
It is clear that regardless of public misperception, the risks from radiation exposure are low.
No human genetic effects have ever been observed even in "worst case scenarios", specifically the detonation of nuclear devices above civilian populations in Hiroshima and Nagasaki, Japan. Specifically:

> *No genetic effects have been detected in a large sample (nearly 80,000) of offspring. By this, we mean that there is no detectable radiation-related increase in congenital abnormalities, mortality (including childhood cancers), chromosome aberrations, or mutations in biochemically identifiable genes.*
>
> ***Health Physics Society – Radiation effects – Hiroshima and Nagasaki - John D. Zimbrick, Ph.D. School of Health Sciences Purdue University***
> *(http://hps.org/publicinformation/ate/q340.html)*

The long term cancer risks in those situations are also low as discussed below:

> *The long-term effects of radiation exposure among the survivors have been extensively studied in what has come to be known as the Life Span Study. (http://www.rerf.jp/index_e.html)The main effect observed has been an excess of approximately 400 cases of cancer among the approximately 100,000 survivors. That means that about 400 more cancers have been observed in this population than would have been expected from a similar, but unexposed population. This excess has been observed among the survivors who received the highest radiation doses (generally, those who were closest to the detonation site).*
>
> ***Health Physics Society – Radiation effects – Hiroshima and Nagasaki - Brant Ulsh, PhD, CHP (http://hps.org/publicinformation/ate/q9122.html)***

Health effects to populations living near the Semipalitinsk Test Site in northeaster Kazakhstan exposed to the effects of nuclear testing are discussed below

> *The results of the analysis of the complex medical examinations have revealed that among the inhabitants of the contaminated areas there were no cases of acute or chronic forms of radiation sickness recorded. It was also noted that all observed deviations in population health were nonspecific for "radiation impact" because deviations were noted both in people living along the nuclear explosion traces and in control settlements. The degree of symptoms does not correlate with exposure doses.*
> *In view of the complete absence of clearly diagnosed cases of acute and chronic forms of radiation sickness, various observed functional changes in the state of the nervous system (asthenovegetative syndrome, asthenic state, vegetative dysfunction) as well as changes in the peripheral blood pattern (leucopenia, leukocytosis, thrombopenia, thrombocytosis, etc.) cannot be considered as changes caused only by the impact of ionizing radiation.*
>
> ***Population Health in Regions Adjacent to the Semipalitinsk Nuclear Test Site - Institute of Biophysics – Russian Federation – Physical Technical Center - Sarov, Russian Federation Published by Armed Forces Radiobiology Research Institute – Bethesda, Maryland – Defense Nuclear Agency (DNA) Contract Number: DNA-001-94-C-0121***

The risks from radiation exposure count as among the best studied and lowest risks among many industrial risks. This is clear from the paper attached in Appendix 1 entitled *Five Hundred Life Saving Interventions and their Cost-Effectiveness.* The data below is from this paper from the section entitled *Radiation control*:

881	Radionuclide emission control at surface uranium mines	$3,900,000
881	Radionuclide emission control at elemental phosphorous plants	$9,200,000
881	Radionuclide emission control at operating uranium mill tailings	$11,000,000
1216	Radionuclide control via best available technology in phosphorous mines	$16,000,000
881	Radionuclide emission control at phosphogypsum stacks	$29,000,000
881	Radionuclide emission control during disposal of uranium mill tailings piles	$40,000,000
1216	Rdiation emission standard for nuclear power plants	$100,000,000
468	Radiation emission standard for nuclear power plants	$180,000,000
926	Thin, flexible, protective leaded gloves for radiologists	$190,000,000
881	Radionuclide emission control at coal-fired industrial boilers	$260,000,000
881	Radionuclide emission control at coal-fired utility boilers	$2,400,000,000
881	Radionuclide emission control at NRC-licensed and non-DOE facilities	$2,600,000,000
881	Radionuclide emission control at uranium fuel cycle facilities	$34,000,000,000

The following are some costs per year of life saved for some non-radiological interventions:

- Grooved pavement on highways $29,000
- Widen existing bridges on highways $82,000
- Dual master cylinder braking systems in cars $13,000
- Cholesterol screening for boys age 10 $6,500
- Influenza vaccination for all citizens $140

Please note that the above costs are in 1995 dollars per year of life saved. The costs per year of life saved for interventions involving radiation are among the highest cost interventions discussed in the paper meaning that the risks from the listed forms of radiation exposure are among the lowest risks studied. An editorial from the Health Physics Society (HPS) Newsletter dated October 1995 about the paper is also included in Appendix 1. The Association agrees with this editorial especially the statement that "*...health physicists should become more aware of the paradox risk analysts have identified, and become more concerned about reducing the cost ineffectiveness of environmental regulations.*"

Low Risks of Radionuclide Emissions Exemplified by the Rescission of 40 CFR part 61 Subpart I

The low risks involved in the emission of radionuclides are exemplified in the rescission of 40 CFR part 61 Subpart I. One of the National Emission Standards for Hazardous Air Pollutants (NESHAPS) was 40 CFR Part 61 Subpart I – *National Emission Standards for Radionuclide Emissions from Facilities Licensed by the Nuclear Regulatory Commission and Federal Facilities Not covered by Subpart H.* This rule established a standard for emissions of radionuclides including iodine to the ambient air not to exceed an amount that would cause any member of the public to receive in any year an effective dose equivalent of 10 mrem/year excluding doses caused by Radon-222 and its decay products formed after the radon is released from a facility.

Subpart I was rescinded by the Environmental Protection Agency (EPA) effective Monday, December 30, 1996 (Federal Register / Volume 61, Number 251 / Monday, December 30, 1996 / Rules and Regulations) and replaced with a constraint rule incorporated into 10 CFR Part 20 (10 CFR Part 20.1101(d)) by the Nuclear Regulatory Commission (NRC) which is as follows:

(d) To implement the ALARA requirements of § 20.1101 (b), and notwithstanding the requirements in § 20.1301 of this part, a constraint on air emissions of radioactive material to the environment, excluding Radon-222 and its daughters, shall be established by licensees other than those subject to § 50.34a,

such that the individual member of the public likely to receive the highest dose will not be expected to receive a total effective dose equivalent in excess of 10 mrem (0.1 mSv) per year from these emissions. If a licensee subject to this requirement exceeds this dose constraint, the licensee shall report the exceedance as provided in § 20.2203 and promptly take appropriate corrective action to ensure against recurrence.

The reason that this was done was the fact that there were ultimately no facilities that exceeded the limits in 40 CFR part 61 Subpart I. This was discussed in preamble to the final rule rescinding Subpart I as follows:
After evaluating both the randomly surveyed 367 facilities and the specifically targeted facilities using the COMPLY computer program, EPA determined that the highest estimated dose received by any member of the public from airborne emissions of radionuclides from any facility was 8.0 mrem/yr ede. Thus, none of the facilities evaluated appeared to cause a dose exceeding the levels established by the Administrator in the radionuclides NESHAPs. The median dose for the population is 0.00069 mrem/yr. See Draft Background Information Document, "NESHAPs Rulemaking on Nuclear Regulatory Licensees Other Than Nuclear Power Reactors" EPA 430–R–92–011 (November 1992), Docket Entry A–92–50, II–B–1 at 4–11. When the results of the survey were statistically extrapolated to the entire population of NRC or Agreement State licensees, EPA concluded that emissions from virtually all of the facilities were expected to be below the limits established by EPA. After evaluating the results of the study, EPA concluded that current emissions by NRC and Agreement State licensees other than nuclear power reactors result in doses less than the level found by EPA to provide an ample margin of safety to protect the public health. The preamble continued by stating:

EPA has previously concluded that radionuclide emissions to the ambient air from NRC and Agreement State licensees other than nuclear power reactors are generally well below the level that would result in a dose exceeding 10 mrem/yr. EPA experience in administration of subpart I since it became effective confirms this conclusion. Out of the thousands of licensees subject to the standard, only 16 facilities reported radionuclide air emissions exceeding the EPA standard for calendar year 1993 and only one facility reported emissions exceeding the EPA standard for calendar year 1994. No facilities reported exceeding the subpart I 10 mrem/yr standard for calendar year 1995. See Memorandum to Docket A–92–50 from Byron Bunger, December 18, 1996, Docket Entry A–92–50, IV–B–2 (Appendix to final rulemaking describing EPA's experience implementing Subpart I). Most of the reported exceedances were resolved through EPA approval of appropriate site-specific adjustments to the input parameters for COMPLY, the computer code used for calculating doses. The one exceedance not resolved through adjustments to the input parameters for COMPLY was satisfactorily resolved by the facility.

The rescission of 40 CFR part 61 Subpart I is an example of the removal of an unneeded regulation, one created by the Environmental Protection Agency (EPA) to regulate a risk (particulate emissions from Nuclear Regulatory Commission (NRC) regulated facilities) that in fact was non-existent. A careful analysis of the risks prior to promulgating the regulation would have led to the realization that it was unneeded. The case of 40 CFR part 61 Subpart I highlights the need for the incorporation of risk management principles in all regulatory endeavors.

Inherent Low Radiological Risks Involved in Uranium Recovery in Particular

The above section described (with appropriate references from the literature) the low risks from radiation exposure even in worst case scenarios. The risks from radiation exposure from uranium recovery operations are very low give the long half lives of most of the radioisotopes involved and their consequent low specific activity. These low activities equate to low doses which in turn equate to low risks.

In addition, the issue of the effects of low radiation doses and the associated risks is open to question. The currently accepted assumption that forms the basis for current radiation protection regulation is the Linear No Threshold Hypothesis (LNT) which assumes that any level of radiation dose no matter how small carries with it a proportionate level of risk of a stochastic effect (cancer). The basis of this dose to risk relationship is based upon relatively high doses of radiation to which atomic bomb survivors, radium watch dial painters and other highly exposed groups received. Doses from uranium recovery facilities are substantially lower and are often indistinguishable from background. This is especially true for doses to members of the public/nearest residents.
Attached in Appendix 2 to this letter please find a paper from Dr. Bernard Cohen now Professor Emeritus of Physics at the University of Pittsburgh entitled *Test of the Linear No-Threshold Theory of Radiation Carcinogenisis for Inhaled Radon Decay Products.* This paper concludes in the abstract:

> *Abstract – Data on lung cancer mortality rates vs. average radon concentration in homes for 1,601 U.S. counties are used to test the linear-no-threshold theory. The widely recognized problems with ecological studies, as applied to this work, are addressed extensively. With or without corrections for variations in smoking prevalence, there is a strong tendency for lung cancer rates to decrease with increasing radon exposure, in sharp contrast to the increase expected from the theory. The discrepancy in slope is about 20 standard deviations. It is shown that uncertainties in lung cancer rates, radon exposures, and smoking prevalence are not important and that confounding by 54 socioeconomic factors, by geography and by altitude and climate can explain only a small fraction of the discrepancy. Effects of known radon-smoking prevalence correlations-rural people have higher radon levels and smoke less than urban people, and smokers are exposed to less radon than non-smokers-are calculated and found to be trivial. In spite of extensive efforts, no potential explanation for the discrepancies other than failure of the linear-no-threshold theory for carcinogensis from inhaled radon decay products could be found.*

It is interesting to note that this paper discussed radon/radon decay product exposure. Radon and radon decay products are the primary isotopes of concern regarding dose to the general public/nearest resident from uranium recovery operations.

The Health Physics Society (HPS) examined the issue of the Linear No-Threshold Hypothesis and requested short papers from experts in the field. This collection of short papers is included in Appendix 3. One included paper discusses the fact that UNSCEAR in 1994 "*...concluded that the data (atom bomb survivor data) could not be used for statistical verification at low doses.*" In addition, in 1994, UNSCEAR acknowledged the existence of hormesis. The existence of any risk from very low doses of radiation is still open to question.

Recently (December 20, 2011) the Lawrence Berkeley National Laboratory released information regarding work performed by researchers there that "*...found evidence to suggest that for low dose levels of ionizing radiation, cancer risks may not be directly proportional to dose. This contradicts the standard model for predicting biological damage from ionizing radiation – the linear-no-threshold hypothesis or LNT – which holds that risk is directly proportional to dose at all levels of irradiation.*"

The press release about this research continued by stating:

"Our data show that at lower doses of ionizing radiation, DNA repair mechanisms work much better than at higher doses," says Mina Bissell, a world-renowned breast cancer researcher with Berkeley Lab's Life Sciences Division. "This non-linear DNA damage response casts doubt on the general assumption that any amount of ionizing radiation is harmful and additive."

This is additional recent research that casts additional doubt on the linear no threshold hypothesis and indicates that the risk from radiation at low doses is less than currently assumed.

The National Institute of Occupational Safety and Health (NIOSH) published a study of uranium mill workers in 2004 which is included in Appendix 4. This paper stated:
Mortality from all causes was less than expected, which is largely accounted for by fewer deaths from heart disease than expected. Mortality from all malignant neoplasms was also less than expected.

The above paper addressed exposures sustained by uranium mill workers.

The following three (3) papers (primary author John D. Boice, Jr. Department of Medicine, Vanderbilt University Medical Center and Vanderbilt Ingram Cancer Center, Nashville, TN 37232, USA) which are included in Appendices 5, 6 and 7 address exposures to residents of counties with substantial uranium processing activity (Karnes county, Texas, Montrose county, Colorado and the area around Grants, New Mexico):

Cancer mortality in a Texas county with prior uranium mining and milling activities, 1950–2001

Cancer and Noncancer Mortality in Populations Living Near Uranium and Vanadium Mining and Milling Operations in Montrose County, Colorado, 1950-2000

A cohort study of uranium millers and miners of Grants, New Mexico, 1979–2005

These papers reach the following conclusions:

> ***Cancer mortality in a Texas county with prior uranium mining and milling activities, 1950–2001***
>
> *The numbers and rates of cancer deaths were determined for Karnes County and for comparison for four 'control' counties in the same region with similar age, race, urbanisation and socioeconomic distributions reported in the 1990US Census. Comparisons were also made with US and Texas general population rates. Following similar methods to those used by the National Cancer Institute, standardised mortality ratios (SMRs) were computed as the ratio of observed numbers of cancers in the study and control counties compared to the expected number derived from general population rates for the United States. Relative risks (RRs) were computed as the ratios of the SMRs for the study and the control counties. Overall, 1223 cancer deaths occurred in the population residing in Karnes County from 1950 to 2001 compared with 1392 expected based on general population rates for the US. There were 3857 cancer deaths in the four control counties during the same 52 year period compared with 4389 expected. There was no difference between the total cancer mortality rates in Karnes County and those in the control counties (RR = 1.0; 95% confidence interval 0.9–1.1). There were no significant increases in Karnes County for any cancer when comparisons were made with either the US population, the State of Texas or the control counties. In particular, deaths due to cancers of the lung, bone, liver and kidney were not more frequent in Karnes County than in the control counties. These are the cancers of a priori interest given that uranium might be expected to concentrate more in these tissues than in others. Further, any radium intake would deposit primarily in the bone and radon progeny primarily in the lung. Deaths from all cancers combined also were not increased in Karnes County and the RRs of cancer mortality in Karnes County before and in the early years of operations (1950–64), shortly after the uranium activities began (1965–79) and in two later time periods (1980–89,*

1990–2001) were similar, 1.0, 0.9, 1.1 and 1.0, respectively. No unusual patterns of cancer mortality could be seen in Karnes County over a period of 50 years, suggesting that the uranium mining and milling operations had not increased cancer rates among residents.

Cancer and Noncancer Mortality in Populations Living Near Uranium and Vanadium Mining and Milling Operations in Montrose County, Colorado, 1950-2000

Between 1950 and 2000, a total or 1,877 cancer deaths occurred in the population residing in Montrose County, compared with 1,903 expected based on general population rates for Colorado (SMR_{CO} 0.99). There' were 11,837 cancer deaths in the five comparison counties during the same 51-year period compared with 12,135 expected (SMRco 0.98). There was no difference between the total cancer mortality rates in Montrose County and those in the comparison counties (RR = 1.01; 95% CI 0.96-1.06). Except for lung cancer among males (RR = 1.19; 95% CI 1.06-1.33), no statistically significant excesses were seen for any causes of death of a priori interest; cancers of the breast, kidney, liver, bone, or childhood cancer, leukemia, non-Hodgkin lymphoma, renal disease or nonmalignant respiratory disease. Lung cancer among females was decreased (RR = 0.83; 95% CI 0.67-1.02). The absence of elevated mortality rates of cancer in Montrose County over a period of 51 years suggests that the historical milling and mining operations did not adversely affect the health of Montrose County residents.

A cohort study of uranium millers and miners of Grants, New Mexico, 1979–2005

No statistically significant elevation in any cause of death was seen among the 904 non-miners employed at the Grants uranium mill. Among 718 mill workers with the greatest potential for exposure to uranium ore, no statistically significant increase in any cause of death of a priori interest was seen, i.e., cancers of the lung, kidney, liver, or bone, lymphoma, non-malignant respiratory disease, renal disease or liver disease. Although the population studied was relatively small, the follow-up was long (up to 50 yrs) and complete.

These three (3) papers show that uranium processing operations in three (3) areas did not increase cancer risks.

In addition, most uranium recovery operations tend to be removed from populated areas. This is true for three (3) recently licensed in-situ uranium recovery operations in Wyoming. . This also lowers the risks to members of the public from these operations.

The Commission itself has acknowledged the low risks related to uranium is-situ recovery in *NUREG-1910 - Generic Environmental Impact Statement for In-Situ Leach Uranium Milling Facilities.* The specific discussion on the risks/impacts of uranium is-situ recovery facilities is included in Appendix 10. The impacts for the most part are considered small.

Specific Response to the Commission's Questions
Common Understanding of Terms

The WMA believes that there is a common understanding of the terms risk-informed, performance-based and defense in depth which is often applied to nuclear reactors. The term risk-informed has been in use by industry, regulators and other stakeholders for many years. Members of the uranium recovery industry

are especially aware of the term risk-informed and are risk-informed themselves clearly understanding that physical safety issues (transportation accidents, slips and falls, falls from height, back injuries, electrical accidents etc.) are the primary risks faced by uranium recovery workers and are greater risks than those from occupational exposure (internal or external) to radiation.

Some members of the uranium recovery industry have possessed performance based licenses for over a decade so there is good understanding of the term "*performance-based*" Performance based licenses consider risk. The Commission allows the licensee's Safety and Environmental Review Panel (SERP to address certain issues on site via a Safety and Environmental Evaluation (SEE) because the risks associated with those actions are less than those requiring a license amendment. These evaluations are then inspected during the facility's routine inspection. Certain items however, can only be authorized via a license amendment from the Commission due to the higher level of risk associated with them. Generally the license amendment authorizing the Safety and Environmental Review Panel (SERP) lists items such as appreciably increasing the frequency of occurrence of an accident previously evaluated in the license application, appreciably increasing the likelihood of occurrence of a malfunction of a structure, system, or component (SSC) important to safety, appreciably increasing the consequences of an accident, appreciably increasing the consequences of a malfunction of an SSC, creating a possibility for an accident of a different type than any previously evaluated, or creating a possibility for a malfunction of an SSC with a different result than previously evaluated as items requiring a license amendment due to the higher level of risk associated with them.

Key Characteristics for a Holistic Risk Management Regulatory Structure

Risk analysis and risk ranking are the key characteristics for a risk management regulatory structure. Risks must be analyzed to determine their magnitude and ranked. Radiological risks should be ranked along with other risks associated with reactors, materials, waste, fuel cycle and security so that it clear where they fit in the overall risk picture. Only then can it be determined where efforts should be best expended to reduce and manage risk. In the case of wastes, the Commission should eliminate arbitrary processed based definitions and define wastes based on the risk they pose which would be based upon their current and long term activity as well as their ability to migrate and/or enter the ecosystem impacti8ng members of the public. Security should also be based upon the activity and associated risk of the materials being secured.

Incorporation of Traditional Deterministic Approaches

Traditional deterministic approaches should be eliminated to the greatest extent possible with materials and processes being evaluated and regulated based upon the risks that they pose.

Challenges of Creating a Holistic Risk Management Regulatory Structure

The WMA believes that the primary challenge will be the issues of perceived versus real risk. Radiation and the handling and/or processing of radioactive materials carries with a large perceived risk especially in the minds of members of the general public in contrast to the actual risk which is very low. The primary challenge will be in overcoming this large perceived risk and educating the general public about the real low risk.

Reasonable Time Period for a Transition to a Risk Management Regulatory Structure

The WMA believes that the transition could be accomplished over a span of five (5) years. This length of time will be required to allow for sufficient industry and public input as well as to develop a consensus on new risk based regulations.

Particular Areas or Issues that Would Benefit the Most by Transitioning to a Risk Management Regulatory Approach

The WMA believes that the following areas of the uranium recovery industry would benefit the most by transitioning to a risk management regulatory approach:

- **Groundwater restoration of in-situ leach wellfields**
  - In-situ leach wellfields are usually within exempted areas of drinking water aquifers (USDWs). Once this area is exempted from the Underground Source of Drinking Water (USDW) it remains forever exempted. The only groundwater restoration that is required is sufficient restoration to ensure that residual contamination within the exempted aquifer does not impact the class of use of the surrounding U.S Drinking Water Aquifer (USDWA). The aquifer itself within the in-situ wellfield generally contains natural Radium-226 as well as generally natural uranium (unless geological conditions (high levels of reduction) prevent the uranium from readily dissolving) to render it unfit for use prior to mining. The portions of the aquifer mined during the in-situ mining process were generally never fit for use due to naturally occurring radionuclides. A rigorous analysis of the risks for proscriptive groundwater restoration of depleted in-situ wellfields (risks of industrial accidents during restoration, consumptive use of groundwater etc.) should be weighed against the benefits of very minimal restoration such as less use of groundwater and less consumption of valuable resources (notably energy) on remediation of an aquifer that was unsuitable for use to begin with due to naturally occurring radionuclides. Background radionuclide activities in groundwater at these sites can be quite high. For example, pre-operational groundwater in and around uranium recovery sites can have very variable and very high concentrations of uranium. Concentrations of uranium in groundwater ranged from .010 to 46 parts per million at the Lost Creek Schroeckingerite area - Sections 1 to 13, Townships 25 and 26 North, Ranges 94 and 95 West in Sweetwater County, Wyoming - *(Geology of the Lost Creek Schroeckingerite Deposits Sweetwater County, Wyoming - Geological Survey Bulletin 1087-J – By Sheridan, Douglas M.; Maxwell, C. H.; Collier, J. T. 1956).* This area is west of UR Energy's recently licensed Lost Creek Project. These high and extremely variable background activities would best be addressed via a risk based approach, since the elevated backgrounds mean that any additional risks presented by any residual radionuclides would be very low.

- **Groundwater remediation of plumes at uranium mill tailings sites**

  Plumes at uranium mill tailings sites eventually fall under Alternate Concentration Limits (ACLs). The lands underlain by these plumes are generally deeded over to the Federal Government (Department of Energy (DOE)) for long term care along with the reclaimed mill tailings impoundment(s). Once deeded to the Federal Government no completion of water wells is permitted in these areas. Without water wells to access these plumes there is no pathway for exposure to humans to the plume thus there is no risk of exposure to the radionuclides in the plume. Without an exposure pathway there is no risk

of exposure. The radionuclides and metals of concern are typically relatively immobile so migration toward an off-site aquifer is unlikely.

Pre-operational groundwater uranium activities can be highly variable and have very high concentrations of uranium. Concentrations of uranium in groundwater ranged from .010 to 46 parts per million at the Lost Creek Schroeckingerite area - Sections 1 to 13, Townships 25 and 26 North, Ranges 94 and 95 West in Sweetwater County, Wyoming which is near both UR Energy's recently licensed Lost Creek Project and Kennecott Uranium Company's Sweetwater Uranium Project (a conventional mill with a tailings impoundment that is currently on standby. - (*Geology of the Lost Creek Schroeckingerite Deposits Sweetwater County, Wyoming - Geological Survey Bulletin 1087-J – By Sheridan, Douglas M.; Maxwell, C. H.; Collier, J. T. 1956*).

The table below shows the variability of natural uranium in various groundwaters:

Rock Type		Uranium Concentration in micrograms per liter			
	Number of Samples	Range	Average	Number of Samples Greater than 4 micrograms per liter	Number of Samples Less than 4 micrograms per liter
Igneous					
Silicic (Light)	33	0 - 32	4.5	12	36
Basic/Intermediary (Dark)	18	0 - 9.2	0.9	1	6
Sedimentary					
Sandstone/Conglomerate	132	0 - 2100	26.2	22	17
Siltstone/shale	14	0 - 69	10.6	6	43
Limestone/dolomite	89	0 - 33	2.0	11	12
Sand/gravel	87	0 - 74	2.5	13	15
Metamorphic					
Undifferentiated	34	0 - 37	4.4	8	24
Totals:	407	0 - 2100	10.6	73	18

Source: *Hydrothermal Uranium Deposits* - Robert A Rich, Heinrich D. Holland and Ulrich Petersen Elsevier Scientific Publishing Company New York 1977

Elevated background radionuclide activities in groundwater coupled with a high variability in background and reduced number of exposure pathways following reclamation mean that a risk based approach would be superior to a deterministic approach in regulating these plumes.

- **Remediation of contaminated soils and establishment of radiological background at sites especially uranium recovery sites where the potential contaminants are also naturally occurring radionuclides.**
    - Remediation of contaminated soils at uranium recovery and other sites, especially deeply buried soils, would benefit from a risk based approach. Risks from buried contaminated soils are minimal especially given the often high background radionuclide activities in sols in uranium recovery areas and the great variability in background.
    - For example, the area around UMETCO's Gas Hills Site had naturally occurring high background. Included in Appendix 8 is background soil sampling data for the area around UMETCO's now reclaimed Gas Hills Mill site. This data was generously provided by UMETCO Minerals Corporation.

- An area to the northwest of Kennecott Uranium company's Sweetwater Uranium Project and UR Energy's recently licensed Lost Creek Project called the Lost Creek Schroeckingerite area (*Sections 1 to 13, Townships 25 and 26 North, Ranges 94 and 95 West in Sweetwater County, Wyoming*) had anomalously high background concentrations of natural uranium and Radium-226. This data is presented in:
    - *Geology of the Lost Creek Schroeckingerite Deposits Sweetwater County, Wyoming* - Geological Survey Bulletin 1087-J – By Sheridan, Douglas M.; Maxwell, C. H.; Collier, J. T. 1956
    - This paper provides near surface trench sampling data for the Lost Creek Area in Sections 1 to 13, Townships 25 and 26 North, Ranges 94 and 95 West in Sweetwater County, Wyoming. This sampling was performed by the United States Geological Survey (USGS) and provides detailed information on the extent of concentrations of naturally occurring radionuclides in soils. All of these samples were collected within fifteen (15) feet of the surface.
    - Detailed sampling data is presented in the publication and is summarized below:

Area	**Average Natural Uranium Activity**	**Average Calculated Radium-226 Activity (Based on measured gamma equivalent uranium activity of the samples)**
	(picocuries per gram)	**(picocuries per gram)**
Lost Creek – Section 1	165.1	56.2
Lost Creek – Sections 2 to 7	324.0	65.1
Lost Creek – Sections 8 to 13	100.4	35.0

- *SECY-03-0069 - RESULTS OF THE LICENSE TERMINATION RULE ANALYSIS* states: Source material (uranium and thorium) is found ubiquitously in nature. The following table describes uranium concentrations in soils:

Uranium Content in Parts per Million (PPM) of Various Sedimentary Rock Types		
Rock Type	**Average Uranium Concentration**	**Range of Uranium Concentration**
Fine grained clastics		
Common shales	3.7	1 - 13
North American gray and green shales	3.2	1.2 - 12
Mancos shale (western U.S.A.)	3.7	0.9 - 12
Black shales		3 - 1250
Coarse grained clastics		
Sandstones		0.45 - 3.2
Orthoquartzites	0.45	0.2 - 0.6
Carbonates		
Carbonate rocks	2.2	0.1 - 9
Russian carbonates	2.1	
North American carbonates	2.2	0.65 - 8.8
California limestones	1.3	0.3 - 4.9

Florida limestones	2	0.5 - 6
Other sedimentary rocks		
Marine phosphorites		50 - 300
Evaporites		0.01 - 0.43
Bentonites	5.0	1 - 21
Bauxites	8.0	3 - 27

Source: *Hydrothermal Uranium Deposits* - Robert A Rich, Heinrich D. Holland and Ulrich Petersen Elsevier Scientific Publishing Company New York 1977

- The above table shows the variability of naturally occurring uranium in soils and rocks. The issue of uncertainties in evaluation of background is discussed in former Commissioner Gail LePlanque's speech *In Search of ... Background* which is attached in Appendix 9. This speech also discusses associated risks.
- Clearly , based on the above discussion of soil sampling data for areas near uranium recovery sites as well as other information provided, background activities of naturally occurring radionuclides (Uranium-238 and its decay products, Uranium-235 and its decay products and Thorium-232 and its decay products) in the natural environment can be quite high and certainly very variable and difficult to predict. Remediation parameters/activities for contaminated soils are often based upon allowing up to a certain activity above a pre-determined background activity to remain. This is a very deterministic approach. It can often create problems, where following the establishment of background radionuclide activities, extremely high background radionuclide activities were discovered during the excavation/remediation process. A radiological risk/dose based remediation standard specific to the site, based upon such considerations as available pathways for exposure should be used instead. If a risk/dose based approach is used for soil remediation it would undoubtedly be much simpler, quicker, involve less excavation of material and also less risk, since the risks of injury to workers from heavy equipment, trips and falls and back injuries exceed those from the very low (at or near background) levels of radiation encountered in the excavation.

- **Establishment of standards for Radon-222 emissions from uranium recovery sites**

  - Radon-222 is ubiquitous in the natural environment. The risks posed by Radon-222 releases from uranium recovery operations are minimal and in the case of some uranium recovery licensees, downwind Radon-222 activities in air can be less than upwind activities. Any Radon-222 contributions from the facility become lost in the variability of background. The Association believes that a risk based approach to addressing Radon-222 emissions from uranium recovery facilities should be implemented.

Conclusions

- The Wyoming Mining Association strongly supports the incorporation of risk management principles and concepts into all regulatory programs and especially for the portions of the programs addressing uranium recovery.
- The WMA believes that risk management principles could most easily and quickly be applied to the following items at uranium recovery sites:
  - Contaminated soil remediation

- Remediation of groundwater plumes related to uranium mill tailings impoundments.
- Restoration of groundwater at uranium in-situ recovery operations.
- Establishment of appropriate background standards for naturally occurring radionuclides in areas of high and/or extremely variable background by basing the standards on a statistical evaluation of background dose.
- Establishment of standards for Radon-222 emissions.

- The WMA believes that these particular items are most suited to risk based approaches because
  - Determination of soil remediation standards, plume remediation standards (groundwater protection standards (GPSs) and restoration parameters for in-situ recovery wellfields are based in part on background standards for the site. Site background can be highly variable and background activities for various radionuclides (natural uranium, Radium-226, and Thorium-230) whether in water or soils can be quite high. A risk/dose based approach would be a superior approach especially since most uranium recovery sites are in remote areas far from residents. Also in many cases there is little of no pathway for exposure from these sites since uranium in-situ recovery occurs within exempted portions of aquifers, groundwater plumes related to uranium mill tailings impoundments are often beneath lands that will be eventually be deeded to the Federal government for long term care and monitoring and areas of remediated contaminated soils at conventional mill sites are also often within lands that will be eventually be deeded to the Federal government for long term care and monitoring.
- The risks in general to radiation exposure are low especially when compared to other risks (motor vehicle operation, alcohol consumption, tobacco use etc.) accepted by society.
- The risks to radiation exposure may be lower than assumed given recent and older work on exposure to low doses of radiation, precisely the same type of low doses associated with uranium recovery.
- The WMA believes that the risks posed by activities involving radioactive material are low and that this is especially the case involving uranium recovery as demonstrated by three (3) epidemiological studies involving populations in areas (Karnes County, Texas, Montrose County, Colorado and the Grants Are in New Mexico).

The Wyoming Mining Association appreciates the opportunity to comments on these issues and appreciates that the Commission is considering the incorporation of risk management concepts in their regulatory programs.

If you have any questions please do not hesitate to contact me.

Sincerely yours,
WYOMING MINING ASSOCIATION

Marion Loomis

Marion Loomis
Executive Director

CC: Katie Sweeney – National Mining Association (NMA)

Appendix 1

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Five-Hundred Life-Saving Interventions and Their Cost-Effectiveness

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We gathered information on the cost-effectiveness of life-saving interventions in the United States from publicly available economic analyses. "Life-saving interventions" were defined as any behavioral and/or technological strategy that reduces the probability of premature death among a specified target population. We defined cost-effectiveness as the net resource costs of an intervention per year of life saved. To improve the comparability of cost-effectiveness ratios arrived at with diverse methods, we established fixed definitional goals and revised published estimates, when necessary and feasible, to meet these goals. The 587 interventions identified ranged from those that save more resources than they cost, to those costing more than 10 billion dollars per year of life saved. Overall, the median intervention costs $42,000 per life-year saved. The median medical intervention costs $19,000/life-year; injury reduction $48,000/life-year; and toxin control $2,800,000/life-year. Cost/life-year ratios and bibliographic references for more than 500 life-saving interventions are provided.

KEY WORDS: Cost-effectiveness; economic evaluation; life-saving; resource allocation.

1. INTRODUCTION

Risk analysts have long been interested in strategies that can reduce mortality risks at reasonable cost to the public. Based on anecdotal and selective comparisons, analysts have noted that the cost-effectiveness of risk-reduction opportunities varies enormously, often over several orders of magnitude.[1-5] This kind of variation is unnerving because economic efficiency in promoting survival requires that the marginal benefit per dollar spent be equal across investments.

Despite continuing interest in cost-effectiveness, we could find no comprehensive and accessible data set on the estimated costs and effectiveness of risk management options. Such a dataset could provide useful comparative information for risk analysts as well as practical information for decision makers who must allocate scarce resources. To this end, we report cost-effectiveness ratios for more than 500 life-saving interventions across all sectors of American society.

2. METHODS

2.1. Literature Review

We performed a comprehensive search for publicly available economic analyses of life-saving interventions.

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"Life-saving interventions" were defined as any behavioral and/or technological strategy that reduces the probability of premature death among a specified target population. To identify analyses we used several on-line databases, examined the bibliographies of textbooks and review articles, and obtained full manuscripts of conference abstracts. Analyses retained for review met the following three criteria: (1) written in the English language, (2) contained information on interventions relevant to the United States, and (3) reported cost per year of life saved, or contained sufficient information to calculate this ratio. Most analyses were scientific journal articles or government regulatory impact analyses, but some were internal government memos, reports issued by research organizations, or unpublished manuscripts.

Two trained reviewers (from a total of 11 reviewers) read each document. Each reviewer recorded 52 items, including detailed descriptions of the nature of the life-saving intervention, the baseline intervention to which it was compared, the target population at risk, and cost per year of life saved. The two reviewers worked independently, then met and came to consensus on the content of the document.

Approximately 1200 documents were identified for retrieval. Of these 1200 documents, 229 met our selection criteria. The 229 documents contained sufficient information for reviewers to calculate cost/life-year saved for 587 interventions.

2.2. Definitional Goals

To increase the comparability of cost-effectiveness estimates drawn from different economic analyses, we established seven definitional goals. When an estimate failed to comply with a goal, reviewers attempted to revise the estimate to improve compliance.[8] In general, reviewers used only the information provided in the document to revise estimates. The seven definitional goals were:

1. Cost-effectiveness estimates should be in the form of "cost per year of life saved." Cost/life saved estimates should be transformed to cost/life-year by considering the average number of years of life saved when a premature death is averted.
2. Costs and effectiveness should be evaluated from the societal perspective.
3. Costs should be "direct." Indirect costs, such as foregone earnings, should be excluded.
4. Costs and effectiveness should be "net." Any resource savings or mortality risks induced by the intervention should be subtracted out.[9]
5. Future costs and life-years saved should all be discounted to their present value at a rate of 5%.
6. Cost-effectiveness ratios should be marginal or "incremental." Both costs and effectiveness should be evaluated with respect to a well-defined baseline alternative.
7. Costs should be expressed in 1993 dollars using the general consumer price index.

[8] Appendices describing the cost-effectiveness formulas used to operationalize these definitional goals, along with some examples of the calculations made by reviewers of the economic analyses, are available from Dr. Tengs.

2.3. Categorization

Interventions were classified according to a four-way typology. (1) Intervention Type (Fatal Injury Reduction, Medicine, or Toxin Control), (2) Sector of Society (Environmental, Health Care, Occupational, Residential, or Transportation), (3) Regulatory Agency (CPSC, EPA, FAA, NHTSA, OSHA, or None), and (4) Prevention Stage (Primary, Secondary, or Tertiary).

Interventions we classified as primary prevention are designed to completely avert the occurrence of disease or injury; those classified as secondary prevention are intended to slow, halt, or reverse the progression of disease or injury through early detection and intervention; and interventions classified as tertiary prevention include all medical or surgical treatments designed to limit disability after harm has occurred, and to promote the highest attainable level of functioning among individuals with irreversible or chronic disease.[6]

3. RESULTS

Cost-effectiveness estimates for more than 500 life-saving interventions appear in Appendix A. This table is separated into three sections according to the type of intervention: Fatal Injury Reduction, Toxin Control, and Medicine. The first column of Appendix A contains the reference number assigned to the document from which the cost-effectiveness estimate was drawn (references are in Appendix B.) The second column contains a very brief description of the life-saving intervention. The

[9] If savings exceed costs, the result could be negative, so that the cost-effectiveness ratio might be ≤$0.

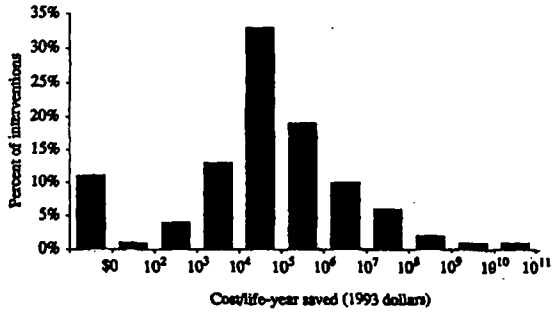

Fig. 1. Distribution of cost/life-year saved estimates (n = 587).

baseline intervention to which the life-saving intervention was compared appears parenthetically as "(vs. ___)" when the author described it. The last column of Appendix A contains the cost per year of life saved in 1993 dollars.

As shown in Fig. 1, these interventions range from those that save more resources than they consume, to those costing more than 10 billion dollars per year of life saved. Furthermore, variation over 11 orders of magnitude exists in almost every category.

In addition to the large variation within categories, variation in cost-effectiveness also exists between categories. As summarized in Table I, while the median intervention described in the literature costs $42,000 per life-year saved (n = 587), the median medical intervention costs $19,000/life-year ($n$ = 310); the median injury reduction intervention costs $48,000/life-year ($n$ = 133); and the median toxin control intervention costs $2,800,000/life-year ($n$ = 144).

Cost-effectiveness also varies as a function of the sector of society in which the intervention is found. For example, as shown in Table I, the median intervention in the transportation sector costs $56,000/life-year saved ($n$ = 87), while the median intervention in the occupational sector costs $350,000/life-year ($n$ = 36). Further dividing occupational interventions into those that avert fatal injuries and those that involve the control of toxins, reveals medians of $68,000/life-year ($n$ = 16) and $1,400,000/life-year ($n$ = 20), respectively.

As noted in Table II, the median cost-effectiveness estimate among those interventions classified as primary prevention is $79,000/life-year saved ($n$ = 373), exceeding secondary prevention at $23,000/life-year ($n$ = 111) and tertiary prevention at $22,000/life-year ($n$ = 103). However, if medicine is considered in isolation, we find that primary prevention is more cost-effective that secondary or tertiary prevention at $5,000/life-year ($n$ = 96).

Table I. Median of Cost/Life-Year Saved Estimates as a Function of Sector of Society and Type of Intervention

	Type of intervention			
Sector of society	Medicine	Fatal injury reduction	Toxin control	All
Health care	$19,000 ($n$=310)	N/A[a]	N/A	$19,000 ($n$=310)
Residential	N/A	$36,000 ($n$=30)	N/A	$36,000 ($n$=30)
Transportation	N/A	$56,000 ($n$=87)	N/A	$56,000 ($n$=87)
Occupational	N/A	$68,000 ($n$=16)	$1,400,000 ($n$=20)	$350,000 ($n$=36)
Environmental	N/A	N/A	$4,200,000 ($n$=124)	$4,200,000 ($n$=124)
All	$19,000 ($n$=310)	$48,000 ($n$=133)	$2,800,000 ($n$=144)	$42,000 ($n$=587)

[a] Not applicable by definition.

Table II. Median of Cost/Life-Year Saved Estimates as a Function of Prevention Stage and Type of Intervention

	Type of intervetion			
Prevention stage	Medicine	Fatal injury reduction	Toxin control	All
Primary	$5,000 ($n$=96)	$48,000 ($n$=133)	$2,800,000 ($n$=144)	$79,000 ($n$=373)
Secondary	$23,000 ($n$=111)	N/A	N/A	$23,000 ($n$=111)
Tertiary	$22,000 ($n$=103)	N/A	N/A	$22,000 ($n$=103)
All	$19,000 ($n$=310)	$48,000 ($n$=133)	$2,800,000 ($n$=144)	$42,000 ($n$=587)

The median cost-effectiveness of proposed government regulations for which we have data also varies considerably. Medians for each agency are as follows: Federal Aviation Administration, $23,000/life-year ($n$ = 4); Consumer Product Safety Commission, $68,000/life-year ($n$ = 11); National Highway Traffic Safety Administration, $78,000/life-year ($n$ = 31); Occupational Safety and Health Administration, $88,000/life-year ($n$ = 16); and Environmental Protection Agency, $7,600,000/life-year ($n$ = 89).

4. LIMITATIONS

This compilation of existing data represents the most ambitious effort ever undertaken to amass cost-effectiveness information across all sectors of society. In

addition, our work to bring diverse estimates into compliance with a set of definitional goals has improved the comparability of cost-effectiveness estimates that were originally derived by different authors using a variety of methods. Nevertheless, several caveats are warranted to aid the reader in interpreting these results.

First, the accuracy of the results presented herein is limited by the accuracy of the data and assumptions upon which the original analyses were based. There remains considerable uncertainty and controversy about the cost consequences and survival benefits of some interventions. This is particularly true for toxin control interventions where authors often extrapolate from animal data. In addition, due to insufficient information in some economic analyses, reviewers were not always successful in bringing estimates into conformity with definitional goals. For example, if the original author did not report the monetary savings due to the reduction in nonfatal injuries requiring treatment, we were unable to "net out" savings, and so the costs used to calculate cost-effectiveness ratios remain gross. While some of these omissions are important, others are largely inconsequential given the relative size of cost and effectiveness estimates.

Second, the life-saving interventions described in this report include those that are fully implemented, those that are only partially implemented, and those that are not implemented at all. These interventions are best thought of as opportunities for investment. While they may offer insight into actual investments in life-saving, the cost-effectiveness of possible and actual investments are not equivalent. Work on the economic efficiency of actual expenditures is in progress.[7]

Third, this dataset may not represent a random sample of all life-saving interventions, so the generalizability of any descriptive statistics may be limited. This is because interventions that have been subjected to economic analysis may not represent a random sample of all life-saving interventions due, for example, to publication bias. That is, those economic analyses that researchers have chosen to perform and journal editors have chosen to publish may be disproportionately expensive or inexpensive. However, the statistics presented herein are certainly applicable to the 587 life-saving interventions in our dataset which by themselves comprise a vast and varied set, worthy of interest even without generalization.

Finally, we recognize that many of these interventions have benefits other than survival, as well as adverse consequences other than costs. For example, interventions that reduce fatal injuries in some people may also reduce nonfatal injuries in others; interventions designed to control toxins in the environment may have short-term effects on survival, but also long-term cumulative effects on the ecosystem; medicine and surgery may increase quantity of life, while simultaneously increasing (or even decreasing) quality of life.

5. CONCLUSIONS

This compilation of available cost-effectiveness data reveals that there is enormous variation in the cost of saving one year of life and these differences exist both within and between categories. Such a result is important because efficiency in promoting survival requires that the marginal benefit per dollar spent be the same across programs. Where there are investment inequalities, more lives could be saved by shifting resources. It is our hope that this information will expand the perspective of risk analysts while aiding future resource allocation decisions.

APPENDIX A. FIVE-HUNDRED LIFE-SAVING INTERVENTIONS AND THEIR COST-EFFECTIVENESS

Ref no.[a]	Life-saving intervention[b]	Cost/life-year[c]
	Fatal injury reduction	
	Airplane safety	
174	Automatic fire extinguishers in airplane lavatory trash receptacles	$16,000
173	Fiberglass fire-blocking airplane seat cushions	$17,000
174	Smoke detectors in airplane lavatories	$30,000
172	Emergency signs, floor lighting etc. (vs. upper lighting only) in airplanes	$54,000
	Automobile design improvements	
190	Install windshields with adhesive bonding (vs. rubber gaskets) in cars	≤ $0
52	Dual master cylinder braking system in cars	$13,000
1128	Automobile dummy acceleration (vs. side door strength) tests	$63,000
299	Collapsible (vs. traditional) steering columns in cars	$67,000
189	Side structure improvements in cars to reduce door intrusion upon crash	$110,000
52	Front disk (vs. drum) brakes in cars	$240,000
299	Dual master cylinder braking system in cars	$450,000
	Automobile occupant restraint systems	
1129	Driver automatic (vs. manual) belts in cars	≤ $0
59	Mandatory seat belt use law	$69
175	Mandatory seat belt use and child restraint law	$98
67	Driver and passenger automatic shoulder belt/knee pads (vs. manual belts) in cars	$1,300
59	Driver and passenger automatic shoulder/manual lap (vs. manual lap) belts in cars	$5,400
67	Airbag/manual lap belts (vs. manual lap belts only) in cars	$6,700
2	Airbag/lap belts (vs. lap/shoulder belts)	$17,000
56	Driver and passenger automatic (vs. manual) belts in cars	$32,000
1129	Driver airbag/manual lap belt (vs. manual lap/shoulder belt) in cars	$42,000
1129	Driver and passenger airbags/manual lap belts (vs. airbag for driver only and belts)	$61,000
59	Driver and passenger airbags/manual lap belts (vs. manual lap belts only) in cars	$62,000
68	Child restraint systems in cars	$73,000
1127	Rear outboard lap/shoulder belts in all (vs. 96%) cars	$74,000
56	Airbags (vs. manual lap belts) in cars	$120,000
1127	Rear outboard and center (vs. outboard only) lap/shoulder belts in all cars	$360,000
	Construction safety	
1137	Full (vs. partial) compliance with 1971 safety standard for concrete construction	≤ $0
1137	1988 (vs. 1971) safety standard for concrete construction	≤ $0
909	1989 (vs. no) safety standard for underground construction	$30,000
909	1989 (vs. 1972) safety standard for underground construction	$30,000
1132	1989 safety standard for underground gassy construction	$30,000
1132	Revised safety standard for underground non-gassy construction	$46,000
106	Install canopies on underground equipment in coal mines	$170,000
910	Safety standard to prevent cave-ins during excavations at construction sites	$190,000
1165	Full compliance with 1989 (vs. partial with 1971) safety standard for trenches	$350,000
1165	Full (vs. partial) compliance with 1971 safety standard for trenches	$400,000
	Fire, heat, and smoke detectors	
193	Federal law requiring smoke detectors in homes	≤ $0
13	Fire detectors in homes	≤ $0
306	Federal law requiring smoke detectors in homes	$920
19	Smoke and heat detectors in homes	$8,100
19	Smoke and heat detectors in bedroom area and basement stairwell	$150,000
303	Smoke detectors in homes	$210,000
	Fire prevention and protection, other	
122	Child-resistant cigarette lighters	$42,000
	Flammability standards	
292	Flammability standard for children's sleepwear size 0–6X	≤ $0
306	Flammability standard for upholstered furniture	$300
292	Flammability standard for children's sleepwear size 7–14	$45,000

APPENDIX A. Continued.

Ref no.[a]	Life-saving intervention[b]	Cost/life-year[c]
372	Flammability standard for upholstered furniture	$68,000
12	Flammability standard for children's sleepwear size 7–14	$160,000
292	Flammability standard for children's clothing size 0–6X	$220,000
292	Flammability standard for children's clothing size 7–14	$15,000,000
Helmet promotion		
31	Mandatory motorcycle helmet laws	≤ $0
186	Federal mandatory motorcycle helmet laws (vs. state determined policies)	$2,000
175	Mandatory motorcycle helmet laws	$2,000
1006	Promote voluntary helmet use while riding All-Terrain Vehicles	$44,000
Highway improvement		
747	Grooved pavement on highways	$29,000
1105	Decrease utility pole density to 20 (vs 40) poles per mile on rural roads	$31,000
747	Channelized turning lanes at highway intersections	$39,000
747	Flashing lights at rail-highway crossings	$42,000
747	Flashing lights and gates at rail-highway crossings	$45,000
747	Widen existing bridges on highways	$82,000
1107	Widen shoulders on rural two-lane roads to 5 (vs. 2) feet	$120,000
1105	Breakaway (vs. existing) utility poles on rural highways	$150,000
1107	Widen lanes on rural roads to 11 (vs. 9) feet	$150,000
1105	Relocate utility poles to 15 (vs. 8) feet from edge of highway	$420,000
Light truck design improvements		
1091	Ceilings of 0–6000 lb light trucks withstand forces of 1.5 × vehicle's weight	$13,000
1091	Ceilings of 0–10,000 lb light trucks withstand forces of 1.5 × vehicle's weight	$14,000
1091	Ceilings of 0–8500 lb light trucks withstand forces of 1.5 × vehicle's weight	$78,000
1091	Ceilings of 0–10,000 lb light trucks withstand 5000 lb of force	$170,000
1126	Side door strength standard in light trucks to minimize front seat intrusion	$190,000
1091	Ceilings of 0–6000 lb light trucks withstand 5000 lb of force	$1,100,000
1126	Side door strength standard in light trucks to minimize back seat intrusion	$10,000,000
Light truck occupant restraint systems		
1089	Driver and passenger nonmotorized automatic (vs. manual) belts in light trucks	$14,000
834	Push-button release and emergency locking retractors on truck and bus seat belts	$14,000
1089	Driver and passenger motorized automatic (vs. manual) belts in light trucks	$50,000
1089	Driver airbag (vs. manual lap/shoulder belt) in light trucks	$56,000
1089	Driver and passenger airbags (vs. manual lap/shoulder belts) in light trucks	$67,000
Natural disaster preparedness		
1221	Soils testing and improved site-grading in landslide-prone areas	≤ $0
1221	Ban residential growth in tsunami-prone areas	≤ $0
710	Strengthen unreinforced masonry San Francisco bldgs to LA standards	$21,000
710	Strengthen unreinforced masonry San Francisco bldgs to beyond LA standards	$1,000,000
1221	Triple the wind resistance capabilities of new buildings	$2,600,000
1221	Construct sea walls to protect against 100-year storm surge heights	$5,500,000
1221	Strengthen buildings in earthquake-prone areas	$18,000,000
School bus safety		
1124	Seat back height of 24" (vs. 20") in school buses	$150,000
1124	Crossing control arms for school buses	$410,000
1124	Signal arms on school buses	$430,000
1124	External loud speakers on school buses	$590,000
1124	Mechanical sensors for school buses	$1,200,000
1124	Electronic sensors for school buses	$1,500,000
1124	Seat belts for passengers in school buses	$2,800,000
1124	Staff school buses with adult monitors	$4,900,000
Speed limit		
9	National (vs. state and local) 55 mph speed limit on highways and interstates	$6,600
175	Full (vs. 50%) enforcement of national 55 mph speed limit	$16,000

APPENDIX A. Continued.

Ref no.[a]	Life-saving intervention[b]	Cost/life-year[c]
353	National (vs. state and local) 55 mph speed limit on highways and interstates	$30,000
185	National (vs. state and local) 55 mph speed limit on highways	$59,000
2	National (vs. state and local) 55 mph speed limit	$89,000
185	National (vs. state and local) 55 mph speed limit on rural interstates	$510,000
Traffic safety education		
175	Driver improvement schools (vs. suspending/revoking license) for bad drivers	≤ $0
175	Media campaign to increase voluntary use of seat belts	$310
175	Public pedestrian safety information campaign	$500
175	Improve traffic safety information for children grades K–12	$710
175	Motorcycle rider education program	$5,700
175	Improve motorcycle testing and licensing system	$8,700
157	Improve basic driver training	$20,000
175	Alcohol safety programs for drunk drivers	$21,000
175	Multimedia retraining courses for injury-prone drivers	$23,000
175	Improve educational curriculum for beginning drivers	$84,000
175	First aid training for drivers	$180,000
1124	Improve pedestrian education programs for school bus passengers grades K-6	$280,000
175	Warning letters sent to problem drivers	$720,000
Vehicle inspection		
864	Random motor vehicle inspection	$1,500
1172	Compulsory annual motor vehicle inspection	$20,000
864	Periodic motor vehicle inspection	$21,000
64	Periodic motor vehicle inspection	$57,000
175	Periodic inspection of motor vehicle sample focusing on critical components	$390,000
175	Periodic motor vehicle inspection	$1,300,000
Injury reduction interventions, miscellaneous		
192	Terminate sale of three-wheeled All-Terrain Vehicles	≤ $0
175	Require front and rear lights to be on when motorcycle is in motion	$1,100
175	Selective traffic enforcement programs at high-risk times and locations	$5,200
217	Insulate omnidirectional CB antennae to avert electrocution	$8,500
311	Oxygen depletion sensor systems for gas space heaters	$13,000
863	Require employers to ensure employees' motor vehicle safety	$25,000
372	"American" oxygen depletion sensor system for gas space heaters	$51,000
1160	Workplace practice standard for electric power generation operation	$59,000
175	Pedestrian and bicycle visibility enhancement programs	$73,000
315	Lock out or tag out of machinery in repair	$99,000
372	"French" oxygen depletion sensor system for gas space heaters	$130,000
1005	Redesign chain saws to reduce rotational kickback injuries	$230,000
101	Ground fault circuit interrupters	$1,100,000
468	Ejection system for the Air Force B-58 bomber	$1,200,000
1161	Equipment, work practices, and training standard for hazardous waste cleanup	$2,000,000
	Toxin control	
Arsenic control		
497	Arsenic emission standard (vs. capture and control) at high-emit copper smelters	$36,000
1216	Arsenic emission control at high-emitting copper smelters	$74,000
497	Arsenic emission standard (vs. capture and control) at glass plants	$2,300,000
1183	Arsenic emission control at low-emitting ASARCO/El Paso copper smelter	$2,600,000
1216	Arsenic emission control at glass plants	$2,900,000
497	Arsenic emission standard (vs. capture and control) at low-emit copper smelters	$3,900,000
881	Arsenic emission control at secondary lead plants	$7,600,000
1216	Arsenic emission control at low-emitting copper smelters	$16,000,000
1183	Arsenic emission control at low-emitting copper smelters	$29,000,000
881	Arsenic emission control at primary copper smelters	$30,000,000
881	Arsenic emission control at glass manufacturing plants	$51,000,000

APPENDIX A. Continued.

Ref no.[a]	Life-saving intervention[b]	Cost/life-year[c]
1183	Arsenic emission control at low-emitting Copper Range/White Pine copper smelter	$890,000,000
Asbestos control		
881	Ban asbestos in brake blocks	$29,000
819	Asbestos exposure standard of 1.0 (vs. 2.0) fibers/cc in asbestos cement industry	$55,000
881	Ban asbestos in pipeline wrap	$65,000
881	Ban asbestos in specialty paper	$80,000
651	Ban products containing asbestos (vs. 0.2 fibers/cc standard)	$220,000
651	Phase in ban of products containing asbestos (vs. 0.2 fibers/cc standard)	$240,000
819	Asbestos exposure standard of 1.0 (vs. 2.0) fibers/cc in textile industry	$400,000
387	Asbestos exposure standard of 0.2 (vs. 2.0) fibers/cc in ship repair industry	$410,000
881	Ban asbestos in roofing felt	$550,000
881	Ban asbestos in friction materials	$580,000
881	Ban asbestos in non-roofing coatings	$790,000
881	Ban asbestos in millboard	$920,000
819	Asbestos exposure standard of 0.2 (vs. 0.5) fibers/cc in friction products industry	$1,200,000
819	Asbestos exposure standard of 0.2 (vs. 0.5) fibers/cc in cement industry	$1,900,000
881	Ban asbestos in beater-add gaskets	$2,000,000
881	Ban asbestos in clutch facings	$2,700,000
881	Ban asbestos in roof coatings	$5,200,000
881	Ban asbestos in sheet gaskets	$5,700,000
881	Ban asbestos in packing	$5,700,000
819	Ban products containing asbestos (vs. 0.5 fibers/cc) in textile industry	$6,800,000
881	Ban asbestos in reinforced plastics	$8,200,000
881	Ban asbestos in high grade electrical paper	$15,000,000
387	Asbestos exposure standard of 0.2 (vs. 2.0) fibers/cc in construction industry	$29,000,000
881	Ban asbestos in thread, yarn, etc.	$34,000,000
819	Asbestos exposure standard of 1.0 (vs. 2.0) fibers/cc in friction products industry	$41,000,000
881	Ban asbestos in sealant tape	$49,000,000
881	Ban asbestos in automatic transmission components	$66,000,000
881	Ban asbestos in acetylene cylinders	$350,000,000
881	Ban asbestos in missile liner	$420,000,000
881	Ban asbestos in diaphragms	$1,400,0000,000
Benzene control		
1139	Benzene exposure standard of 1 (vs. 10) ppm in rubber and tire industry	$76,000
881	Control of new benzene fugative emissions	$230,000
881	Control of existing benzene fugative emissions	$240,000
721	Benzene exposure standard of 1 (vs. 10) ppm	$240,000
881	Benzene emission control at pharmaceutical manufacturing plants	$460,000
881	Benzene emission control at coke by-product recovery plants	$1,400,000
1139	Benzene exposure standard of 1 (vs. 10) ppm in coke and coal chemicals industry	$3,000,000
881	Benzene emission control during transfer operations	$4,100,000
881	Control of benzene storage vessels	$14,000,000
881	Benzene emission control at ethylbenzene/styrene process vents	$14,000,000
881	Benzene emission control during waste operations	$19,000,000
881	Benzene emission control at maleic anhydride plants	$20,000,000
881	Benzene emission control at service stations storage vessels	$91,000,000
881	Control of benzene equipment leaks	$98,000,000
881	Benzene emission control at chemical manufacturing process vents	$180,000,000
881	Benzene emission control at bulk gasoline plants	$230,000,000
881	Benzene emission control at chemical manufacturing process vents	$530,000,000
881	Benzene emission control at rubber tire manufacturing plants	$20,000,000,000
Chlorination		
42	Chlorination of drinking water	$3,100
42	Chlorination, filtration and sedimentation of drinking water	$4,200
Coal and coke oven emissions control		
38	Coal-fired power plants emission control through high stacks etc.	≤ $0

APPENDIX A. Continued.

Ref no.[a]	Life-saving intervention[b]	Cost/life-year[c]
38	Coal-fired power plants emission control through coal beneficiation etc.	$37,000
745	Coke oven emission standard for iron- or steel-producing plants	$130,000
745	Acrylonitrile emission control via best available technology	$9,000,000
Formaldehyde control		
716	Ban urea-formaldehyde foam insulation in homes	$11,000
311	Ban urea-formaldehyde foam insulation in homes	$220,000
1164	Formaldehyde exposure standard of 1 (vs. 3) ppm in wood industry	$6,700,000
Lead control		
1217	Reduced lead content of gasoline from 1.1 to 0.1 grams per leaded gallon	≤ $0
1,3 Butadiene control		
1138	1,3 Butadiene exposure standard of 10 (vs. 1000) ppm PEL in polymer plants	$340,000
1138	1,3 Butadiene exposure standard of 2 (vs. 1000) ppm PEL in polymer plants	$770,000
Pesticide control		
713	Ban chlorobenzilate pesticide on noncitrus	≤ $0
403	Ban amitraz pesticide on apples	≤ $0
403	Ban amitraz pesticide on pears	$350,000
713	Ban chlorobenzilate pesticide on citrus	$1,200,000
Pollution control at paper mills		
844	Chloroform emission standard at 17 low cost pulp mills	≤ $0
844	Chloroform private well emission standard at 7 papergrade sulfite mills	$25,000
844	Chloroform private well emission standard at 7 pulp mills	$620,000
844	Chloroform reduction by replacing hypochlorite with chlorine dioxide at 1 mill	$990,000
844	Dioxin emission standard of 5 lbs/air dried ton at pulp mills	$4,500,000
844	Dioxin emission standard of 3 (vs. 5) lbs/air dried ton at pulp mills	$7,500,000
844	Chloroform emission standard of 0.001 (vs. 0.01) risk level at pulp mills	$7,700,000
844	Chloroform reduction by replace hypochlorite with chlorine dioxide at 70 mills	$8,700,000
844	Chloroform reduction at 70 (vs. 33 worst) pulp and paper mills	$15,000,000
844	Chloroform reduction at 33 worst pulp and paper mills	$57,000,000
844	Chloroform private well emission standard at 48 pulp mills	$99,000,000,000
Radiation control		
468	Automatic collimators on X-ray equipment to reduce radiation exposure	$23,000
881	Radionuclide emission control at underground uranium mines	$79,000
881	Radionuclide emission control at Department of Energy facilities	$730,000
1216	Radionuclide control via best available technology in uranium mines	$850,000
44	Radiation standard "as low as reasonably achievable" for nuclear power plants	$1,100,000
468	Radiation levels of 0.3 (vs. 1.0) WL at uranium mines	$1,600,000
1215	Radiation standard "as low as reasonably achievable" for nuclear power plants	$2,500,000
881	Radionuclide emission control at surface uranium mines	$3,900,000
881	Radionuclide emission control at elemental phosphorous plants	$9,200,000
881	Radionuclide emission control at operating uranium mill tailings	$11,000,000
1216	Radionuclide control via best available technology in phosphorous mines	$16,000,000
881	Radionuclide emission control at phosphogypsum stacks	$29,000,000
881	Radionuclide emission control during disposal of uranium mill tailings piles	$40,000,000
1216	Rdiation emission standard for nuclear power plants	$100,000,000
468	Radiation emission standard for nuclear power plants	$180,000,000
926	Thin, flexible, protective leaded gloves for radiologists	$190,000,000
881	Radionuclide emission control at coal-fired industrial boilers	$260,000,000
881	Radionuclide emission control at coal-fired utility boilers	$2,400,000,000
881	Radionuclide emission control at NRC-licensed and non-DOE facilities	$2,600,000,000
881	Radionuclide emission control at uranium fuel cycle facilities	$34,000,000,000

APPENDIX A. Continued.

Ref no.[a]	Life-saving intervention[b]	Cost/life-year[c]
	Radon control	
1266	Radon remediation in homes with levels ≥ 21.6 pCi/L	$6,100
1267	Radon remediation in homes with levels ≥ 8.11 pCi/L	$35,000
1030	Radon limit after disposal of uranium mill tailings of 20 (vs. 60) p(i/m2s)	$49,000
1265	Radon remediation in homes with levels ≥ 4 pCi/L	$140,000
1030	Radon limit after disposal of uranium mill tailings of 2 (vs. 6) p(i/m2s)	$260,000
881	Radon emission control at Department of Energy facilities	$5,100,000
	SO2 control	
923	SO2 controls by installation of capacity to desulphurize residual fuel oil	≤ $0
	Trichloroethylene control	
1215	Trichloroethylene standard of 2.7 (vs. 11) microgram/L in drinking water	$34,000,000
	Vinyl chloride control	
881	Vinyl chloride emission control at EDC/VC and PVC plants	$1,600,000
718	Vinyl chloride emission standard	$1,700,000
	VOC control	
1122	South Coast of California ozone control program	$610,000
	Toxin control, miscellaneous	
725	Process safety standard for management of hazardous chemicals	$77,000
	Medicine	
	Alpha antitrypsin replacement therapy	
1004	Alpha antitrypsin replacement (vs. med) therapy for smoking men age 70	$31,000
1004	Alpha antitrypsin replacement (vs. med) therapy for smoking women age 40	$36,000
1004	Alpha antitrypsin replacement (vs. med) therapy for nonsmoking women age 30	$56,000
1004	Alpha antitrypsin replacement (vs. med) therapy for nonsmoking men age 60	$80,000
	Beta-blocker treatment following myocardial infarction	
952	Beta blockers for myocardial infarction survivors with no angina or hypertension	$360
952	Beta-blockers for myocardial infarction survivors	$850
176	Beta-blockers for high-risk myocardial infarction survivors	$3,000
176	Beta-blockers for low-risk myocardial infarction survivors	$17,000
	Breast cancer screening	
142	Mammography for women age 50	$810
283	Mammography every 3 years for women age 50–65	$2,700
658	Annual mammography and breast exam for women age 35–49	$10,000
658	Annual physical breast cancer exam for womena age 35–49	$12,000
611	Annual mammography and breast exam (vs. just exam) for women age 40–64	$17,000
1230	Annual mammography and breast exam for women age 40–49	$62,000
1230	Annual mammography and breast exam (vs. just exam) for women age 40–49	$95,000
86	Annual mammography for women age 55–64	$110,000
1230	Annual mammography (vs. current screening practices) for women age 40–49	$190,000
	Breast cancer treatment	
1238	Postsurgical chemotherapy for premenopausal women with breast cancer	$18,000
1238	Postsurgical chemotherapy for women with breast cancer age 60	$22,000
1269	Bone marrow transplant and high (vs. standard) chemotherapy for breast cancer	$130,000
	Cervical cancer screening	
1316	Cervical cancer screening every 3 years for women age 65+	≤ $0
120	Cervical cancer screening every 9 (vs. 10) years for women age 30–39	$410
618	One time mass screening for cervical cancer for women age 38	$1,200
1316	Cervical cancer screening every 5 years for women age 65+	$1,900
1316	One time cervical cancer screening for women age 65+	$2,100

APPENDIX A. Continued.

Ref no.[a]	Life-saving intervention[b]	Cost/life-year[c]
120	Cervical cancer screening every 2 (vs. 3) years for women age 30–39	$2,300
1316	Cervical cancer screening every 3 years for women age 65+	$2,800
120	Annual (vs. every 2 years) cervical cancer screening for women age 30–39	$4,100
783	One time cervical cancer screening for never-screened poor women age 65	$5,000
707	Annual cervical cancer screening for women beginning at age 60	$11,000
81	Cervical cancer screening every 4 years (vs. never) for women age 20	$12,000
88	One time mass screening for cervical cancer	$13,000
258	Cervical cancer screening every 5 years for women age 35+ with 3+ kids	$32,000
1316	Cervical cancer screening every 3 years for regularly-screened women age 65+	$41,000
1316	Annual (vs. every 3 years) cervical cancer screening for women age 65+	$49,000
707	Annual cervical cancer screening for women beginning at age 21	$50,000
603	Annual cervical cancer screening for women beginning at age 20	$82,000
81	Cervical cancer screening every 3 (vs. 4) years for women age 20	$220,000
456	Annual cervical cancer screening for women beginning at age 20	$220,000
81	Cervical cancer screening every 2 (vs. 3) years for women age 20	$310,000
81	Annual (vs. every 2 years) cervical cancer screening for women age 20	$1,500,000
Childhood immunization		
65	Immunization for all infants and pre-school children (vs. scattered efforts)	≤ $0
143	Pertussis, diphtheria, and tetanus (vs. just diphtheria and tetanus) immunization	≤ $0
349	Measles, mumps, and rubella immunization for children	≤ $0
812	Polio immunization for children age 0–4	≤ $0
812	Rubella vaccination for children age 2	≤ $0
1178	National measles eradication program for children	≤ $0
Cholesterol screening		
605	Cholesterol screening for boys age 10 and their first-degree relatives	$4,600
605	Cholesterol screening for boys age 10	$6,500
Cholesterol treatment		
1071	Lovastatin for men age 35–54 with heart disease and ≥ 250 mg/dL	≤ $0
785	Low-cholesterol diet for men age 60 and 180 mg/dL	$12,000
2	Low-cholesterol diet for men age 30	$19,000
1071	Lovastatin for men age 55–64 with heart disease and < 250 mg/dL	$20,000
791	Oat bran cholesterol reduction for men age 48 and > 265 mg/dL	$24,000
785	Lovastatin/low cholesterol diet (vs. diet) for men age 60 and 300 mg/dL	$26,000
785	Cholestyramine/low cholesterol diet (vs. diet) for men age 60 and 300 mg/dL	$31,000
1071	Lovastatin for men age 45–54 with no heart disease and ≥ 300 mg/dL	$34,000
768	Cholestyramine/low cholesterol diet (vs. diet) for age 35–39 and 290 mg/dL	$100,000
768	Cholestyramine/low cholesterol diet (vs. diet) for men age 50–54 and 290 mg/dL	$150,000
791	Cholestyramine for men age 48 and > 265 mg/dL	$160,000
768	Cholestyramine/low cholesterol diet (vs. cholestyramine) age 35–39 290 mg/dL	$200,000
1191	Cholestyramine for men with cholesterol levels above the 95th percentile	$230,000
785	Low-cholesterol diet for men age 20 and 180 mg/dL	$360,000
1071	Lovastatin 40 (vs. 20) mg for women age 35–44 with heart disease < 250 mg/dL	$360,000
768	Cholestyramine/low cholesterol diet (vs. diet) for men age 65–69 and 290 mg/dL	$920,000
1071	Lovastatin for women age 35–44 with no heart disease and ≥ 300 mg/dL	$1,200,000
785	Cholestyramine/low cholesterol diet (vs. diet) for men age 20 and 240 mg/dL	$1,300,000
785	Cholestyramine/low cholesterol diet (vs. diet) for men age 20 and 240 mg/dL	$1,800,000
Clinical trials		
1134	Women's Health Trial to evaluate low-fat diet in reducing breast cancer	$18,000
1004	Clinical trial to evaluate alpha antitrypsin replacement therapy	$53,000
Colorectal screening		
86	Annual stool guaiac colon cancer screening for people age 55+	≤ $0
96	One stool guaiac colon cancer screening for people age 40+	$660
528	One hemoccult screening for colorectal cancer for asymptomatic people age 55	$1,300
1135	Colorectal cancer screening for people age 40+	$4,500
1135	Colonoscopy for colorectal cancer screening for people age 40+	$90,000
96	Six (vs. five) stool guaiacs colon cancer screening for people age 40+	$26,000,000

APPENDIX A. Continued.

Ref no.[a]	Life-saving intervention[b]	Cost/life-year[c]
	Coronary artery bypass graft surgery (CABG)	
358	Left main coronary artery bypass graft surgery (vs. medical management)	$2,300
99	Left main coronary artery bypass graft surgery (vs. medical management)	$5,600
99	3-vessel coronary artery bypass graft surgery (vs. medical management)	$12,000
1200	3-vessel coronary artery bypass graft surgery (vs. PTCA) for severe angina	$23,000
358	2-vessel coronary artery bypass graft surgery (vs. medical management)	$28,000
99	2-vessel coronary artery bypass graft surgery (vs. medical management)	$75,000
1200	3-vessel coronary artery bypass graft surgery (vs. PTCA) for mild angina	$100,000
1200	2-vessel coronary artery bypass graft surgery (vs. PTCA) for severe angina	$430,000
	Drug and alcohol treatment	
86	Occupational assistance programs for working problem-drinkers	≤ $0
650	Detoxification for heroin addicts	≤ $0
650	Methadone maintenance for heroin addicts	≤ $0
650	Narcotic antagonists for heroin addicts	≤ $0
	Emergency vehicle response	
987	Defibrillators in emergency vehicles for resuscitation after cardiac arrest	$39
987	Defibrillators in emergency vehicles staffed with paramedics (vs. EMTs)	$390
986	Defibrillators in ambulances for resuscitation after cardiac arrest	$460
987	Emergency vehicle response for cardiac arrest	$820
2	Advanced life support paramedical equipped vehicle	$5,400
237	Advanced resuscitative care (vs. basic emergency services) for cardiac arrest	$27,000
175	Combined emergency medical services for coordinated rapid response	$120,000
	Gastrointestinal screening and treatment	
578	Sclerotherapy (vs. medical therapy) for esophageal bleeding in alcoholics	≤ $0
148	Truss (vs. elective inguinal herniorrhaphy) for inguinal hernia in elderly patients	≤ $0
352	Expectant management of silent gallstones in men age 30	≤ $0
797	Home (vs. hospital) parenteral nutrition for patients with acute loss of bowels	≤ $0
797	Home parenteral nutrition for patients with acute loss of bowels	≤ $0
584	Pre-operative total parenteral nutrition in gastrointestinal cancer patients	≤ $0
235	Ulcer therapy (vs. surgery) for duodenal ulcers	$6,600
577	Medical or surgical treatment for advanced esophageal cancer	$12,000
587	Surgery for liver cirrhosis patients with acute variceal bleeding	$17,000
1046	Ulcer (vs. symptomatic) therapy for episodic upper abdomen discomfort	$41,000
1067	Misoprostol to prevent drug-induced gastrointestinal bleed in at-risk patients	$47,000
587	Medical management for liver cirrhosis patients with acute variceal bleeding	$61,000
1067	Misoprostol to prevent drug-induced gastrointestinal bleed	$210,000
1046	Upper gastrointestinal X-ray and endoscopy (vs. ulcer therapy) for gastric cancer	$300,000
1046	Upper gastrointetinal X-ray and endoscopy (vs. antacids) for gastric cancer	$420,000
	Heart disease screening and treatment, miscellaneous	
518	Exercise stress test for asymptomatic men age 60	$40
358	Pacemaker implant (vs. medical management) for atrioventricular heart block	$1,600
251	Reconstruct mitral valve for symptomatic mitral valve disease	$6,700
350	Exercise stress test for age 60 with mild pain and no left ventricular dysfunction	$13,000
990	Implantable cardioverter-defibrillator (vs. medical therapy) for cardiac arrest	$23,000
1066	Coronary angiogaphy (vs. medical therapy) in men age 45–64 with angina	$28,000
346	Regular leisure time physical activity, such as jogging, in men age 35	$38,000
251	Replace (vs. reconstruct) mitral valve for symptomatic mitral valve disease	$150,000
	Heart transplantation	
544	Heart transplantation for patients age 55 or younger and favorable prognosis	$3,600
835	*Heart transplantation for patients age 50 with terminal heart disease*	$100,000
	HIV/AIDS screening and prevention	
6	Voluntary (vs. limited) screening for HIV in female drug users and sex partners	≤ $0
1097	Screen blood donors for HIV	$14,000
1100	Screen donated blood for HIV with an additional FDA-licensed test	$880,000

APPENDIX A. Continued.

Ref no.[a]	Life-saving intervention[b]	Cost/life-year[c]
1102	Universal (vs. category-specific) precautions to prevent HIV transmission	$890,000
HIV/AIDS treatment		
1199	Zidovudine for asymptomatic HIV+ people	≤ $0
1121	Oral dapsone for prophylaxis of PCP in HIV+ people	$16,000
1121	Aerosolized pentamidine for prophylaxis of PCP in HIV+ people	$20,000
1096	AZT for people with AIDS	$26,000
1264	Prophylactic AZT following needlestick injury in health care workers	$41,000
1117	Zidovudine for asymptomatic HIV+ people	$45,000
Hormone replacement therapy		
227	Estrogen for menopausal women age 50	≤ $0
748	Estrogen-progestin for symptomatic monopausal women age 50	$15,000
748	Estrogen for symptomatic menopausal women age 50	$26,000
748	Estrogen-progestin for 15 years in asymptomatic menopausal women age 50	$30,000
748	Estrogen-progestin for 5 years in asymptomatic menopausal women age 50	$32,000
90	Estrogen for post-menopausal women age 55–70	$36,000
227	Estrogen for menopausal women age 50	$42,000
90	Estrogen for asymptomatic post-menopausal women age 50–65	$77,000
90	Estrogen for symptomatic post-menopausal women age 50–65	$81,000
748	Estrogen for asymptomatic menopausal women age 50	$89,000
244	Hormone replacement for asymptomatic perimenopausal white women age 50	$120,000
227	Estrogen-progestin for post-menopausal women age 60	$130,000
90	Estrogen for asymptomatic post-menopausal women age 55–70	$250,000
Hypertension drugs		
225	Antihypertensive drugs for men age 25+ and 125 mmHg	$3,800
225	Antihypertensive drugs for men age 25+ and 85 mmHg	$4,700
1068	Beta-blockers for hypertensive patients age 35–64 no heart disease and ≥ 95 mmHg	$14,000
91	Antihypertensive drugs for patients age 40 and ≥ 105 mmHg	$16,000
91	Antihypertensive drugs for patients age 40 and 95–104 mmHg	$32,000
1068	Captopril for people age 35–64 with no heart disease and ≥ 95 mmHg	$93,000
Hypertension screening		
111	Hypertension screening for Black men age 55–64 and ≥ 90 mmHg	$5,000
761	Hypertension screening for men age 45–54	$5,200
111	Hypertension screening for White men age 45–54 and ≥ 90 mmHg	$6,500
111	Hypertension screening for Black women age 45–54 and ≥ 90 mmHg	$8,400
1202	Hypertension screening for asymptomatic men age 60	$11,000
1202	Hypertension screening for asymptomatic women age 60	$17,000
1202	Hypertension screening for asymptomatic men age 40	$23,000
761	Hypertension screening every 5 years for men age 55–64	$31,000
1202	Hypertension screening for asymptomatic women age 40	$36,000
111	Hypertension screening for White women age 18–24 and ≥ 90 mmHg	$37,000
1202	Hypertension screening for asymptomatic men age 20	$48,000
1202	Hypertension screening for asymptomatic women age 20	$87,000
Hysterectomy to prevent uterine cancer		
750	Hysterectomy without oopherectomy for asymptomatic women age 35	≤ $0
750	Hysterectomy with oopherectomy for asymptomatic women age 40	$51,000
758	Hysterectomy for asymptomatic women age 35	$230,000
Influenza vaccination		
455	Influenza vaccination for all citizens	$140
156	Influenza vaccination for high risk people	$570
156	Influenza vaccination for people age 5+	$1,300
Intensive care		
422	Coronary care unit for patients under age 65 with cardiac arrest	$390
125	Intensive care for young patients with barbiturate overdose	$490
1208	Intensive care and mechanical ventilation for acute respiratory distress syndrome	$3,100

APPENDIX A. Continued.

Ref no.[a]	Life-saving intervention[b]	Cost/life-year[c]
125	Intensive care for young patients with polyradiculitis	$3,600
1208	Intensive care and mechanical ventilation for acute respiratory failure	$4,700
854	Intensive care for unstable patients with unpredictable clinical course	$21,000
1208	Intensive care for patients with heart disease and respiratory failure	$21,000
125	Intensive care for patients with multiple trauma	$26,000
89	Coronary care unit for emergency patients with acute chest pain	$250,000
602	Intensive care for very ill patients undergoing major vascular surgery	$300,000
602	Intensive care for very ill patients with operative complications	$390,000
602	Intensive care for seriously ill patients with multiple trauma	$460,000
602	Intensive care for very ill patients undergoing neurosurgery for head trauma	$490,000
125	Intensive care for men with advanced cirrhosis, kidney and liver failure	$530,000
602	Intensive care for very ill patients with emergency abdominal catastrophes	$660,000
602	Intensive care for very ill patients undergoing neoplastic disease operations	$820,000
602	Intensive care for very ill patients undergoing major vascular operations	$850,000
602	Intensive care for very ill patients with gastrointestinal bleeding, cirhosis etc.	$950,000
Leukemia treatment and infection control		
1095	Bone marrow transplant (vs. chemotherapy) for acute nonlymphocytic leukemia	$12,000
1095	Bone marrow transplant for acute nonlymphocytic leukemia in adults	$20,000
1095	Chemotherapy for acute nonlymphocytic leukemia in adults	$27,000
672	Therapeutic leukocyte transfusion to prevent infection during chemotherapy	$36,000
672	Prophylactic (vs. therapeutic) leukocyte transfusion to prevent infection	$210,000
1239	Intravenous immune globulin to prevent infections in leukemia patients	$7,100,000
Neonatal intensive care		
335	Neonatal intensive care for infants weighing 1000–1499 grams	$5,700
83	Neonatal intensive care for infants weighing 751–1000 grams	$5,800
335	Neonatal intensive care for infants weighing 500–999 grams	$18,000
1249	Neonatal intensive care for low birth weight infants	$270,000
Newborn screening		
1195	PKU genetic disorder screening in newborns	≤ $0
1196	Congenital hypothyroidism screening in newborns	≤ $0
1141	Sickle cell screening for Black newborns	$240
1141	Sickle cell screening for non-Black high risk newborns	$110,000[d]
1141	Sickle cell screening for newborns	$65,000,000
1141	Sickle cell screening for non-Black low risk newborns	$34,000,000,000
Organized health services		
1249	Special supplemental food program for women, infants, and children	$3,400
653	Comprehensive (vs. fragmented) health care services	$5,700
653	Comprehensive (vs. fragmented) health care services for mothers and children	$11,000
1249	Organized family planning services for teenagers	$16,000
1191	No cost-sharing (vs. cost sharing) for health care services	$74,000
1249	Community health care services for women and infants	$100,000
Osteoporosis screening		
244	Bone mass screening and treat if < 0.9 g/(cm)^2 for perimenopausal women age 50	$13,000
244	Bone mass screening and treat if < 1.0 g/(cm)^2 for perimenopausal women age 50	$18,000
244	Bone mass screening and treat if < 1.1 g/(cm)^2 for perimenopausal women age 50	$41,000
Percutaneous transluminal coronary angioplasty (PTCA)		
358	PTCA (vs. medical management) for men age 55 with severe angina	$5,300
1200	PTCA (vs. medical management) for men age 55 with severe angina	$7,400
358	PTCA (vs. medical management) for men age 55 with mild angina	$24,000
1200	PTCA (vs. medical management) for men age 55 with mild angina	$110,000
Pneumonia vaccination		
812	Pneumonia vaccination for people age 65+	$1,800
782	Pneumonia vaccination for people age 65+	$2,000
347	Pneumonia vaccination for people age 65+	$2,200

APPENDIX A. Continued.

Ref no.[a]	Life-saving intervention[b]	Cost/life-year[c]
693	Pneumonia vaccination for people age 65+	$2,200
812	Pneumonia vaccination for high risk immunodeficient people age 65+	$6,500
812	Pneumonia vaccination for people age 45–64	$10,000
782	Pneumonia vaccination for high risk people age 25–44	$14,000
812	Pneumonia vaccination for high risk immunodeficient people age 45–64	$28,000
782	Pneumonia vaccination for low risk people age 25–44	$66,000
782	Pneumonia vaccination for children age 2–4	$160,000
347	Pneumonia vaccination for children age 2–4	$170,000
693	Pneumonia vaccination for children age 2–4	$170,000
Prenatal care		
1253	Term guard uterine activity monitor (vs. self-palpation) to detect contractions	≤ $0
924	Financial incentive of $100 to seek prenatal care for low risk women	≤ $0
1250	Universal (vs. existing) prenatal care for women with < 12 years of education	≤ $0
1250	Universal (vs. existing) prenatal care for women with > 12 years of education	≤ $0
1250	Universal (vs. existing) prenatal care for women with 12 years of education	≤ $0
1251	Prenatal screening for hepatitis B in high risk women	≤ $0
1220	Brady method screening for group B streptococci colonization during labor	≤ $0
1256	Prenatal care for pregnant women	≤ $0
340	Antepartum Anti-D treatment for Rh-negative primiparae pregnancies	$1,100
1249	Prenatal care for pregnant women	$2,100
340	Antepartum Anti-D treatment for Rh-negative multiparae pregnancies	$2,900
1220	Isada method screening for group B streptococci colonization during labor	$5,000
Renal dialysis		
801	Home dialysis for chronic end-stage renal disease	$20,000
1049	Home dialysis for end-stage renal disease	$22,000
157	Home dialysis for end-stage renal disease	$23,000
139	Home dialysis for people age 45 with chronic renal disease	$24,000
419	Home dialysis for people age 64 or younger with chronic renal disease	$25,000
1049	Hospital dialysis for end-stage renal disease	$31,000
418	Home dialysis for people age 55–60 with acute renal failure	$32,000
357	Dialysis for people age 35 with end-stage renal disease	$38,000
419	Hospital dialysis for people age 55–64 with chronic renal failure	$42,000
689	Home dialysis for end-stage renal disease	$46,000
418	Hospital dialysis for people age 55–60 with acute renal failure	$47,000
342	Dialysis for end-stage renal disease	$51,000
1049	Center dialysis for end-stage renal disease	$55,000
1050	Center dialysis for end-stage renal disease	$63,000
157	Center dialysis for end-stage renal disease	$64,000
139	Center dialysis for people age 45 with chronic renal disease	$67,000
801	Center dialysis for end-stage renal disease	$68,000
689	Center dialysis for end-stage renal disease	$71,000
342	Hospital dialysis for end-stage renal disease	$74,000
689	Home dialysis (vs. transplantation) for end-stage renal disease	$79,000
Renal dialysis and transplantation		
689	Home dialysis then transplant for end-stage renal disease	$40,000
689	Hospital dialysis then transplant for end-stage renal disease	$46,000
Renal transplantation and infection control		
1065	Cytomegalovirus immune globulin to prevent infection after renal transplant	$3,500
1065	Cytomegalovirus immune globulin to prevent infection after renal transplant	$14,000
157	Kidney transplant for end-stage renal disease	$17,000
419	Kidney transplant and dialysis for people age 15–34 with chronic renal failure	$17,000
139	Kidney transplant for people age 45 with chronic renal disease	$19,000
1050	Kidney transplant from live-related donor for end-stage renal disease	$19,000
357	Kidney transplant from cadaver with cyclosporine (vs. azathioprine)	$27,000
357	Kidney transplant from cadaver with cyclosporine	$29,000
357	Kidney transplant from cadaver with azathioprine	$29,000

APPENDIX A. Continued.

Ref no.[a]	Life-saving intervention[b]	Cost/life-year[c]
1065	Cytomegalovirus immune globulin to prevent infection after renal transplant	$200,000
Smoking cessation advice		
1185	Smoking cessation advice for pregnant women who smoke	≤ $0
952	Smoking cessation among patients hospitalized with myocardial infarction	≤ $0
773	Smoking cessation advice for men age 50–54	$990
773	Smoking cessation advice for men age 45–49	$1,100
773	Smoking cessation advice for men age 35–39	$1,400
773	Smoking cessation advice for women age 50–54	$1,700
773	Smoking cessation advice for women age 45–49	$1,900
773	Smoking cessation advice for women age 35–39	$2,900
771	Nicotine gum (vs. no gum) and smoking cessation advice for men age 45–49	$5,800
119	Nicotine gum (vs. no gum) and smoking cessation advice for men age 35–69	$7,500
771	Nicotine gum (vs. no gum) and smoking cessation advice for men age 65–69	$9,100
771	Nicotine gum (vs. no gum) and smoking cessation advice for women age 50–54	$9,700
86	Smoking cessation advice for people who smoke more than one pack per day	$9,800
119	Nicotine gum (vs. no gum) and smoking cessation advice for women age 35–69	$11,000
771	Nicotine gum (vs. no gum) and smoking cessation advice for women age 65–69	$13,000
Tuberculosis treatment		
784	Isoniazid chemotherapy for high risk White male tuberculin reactors age 20	≤ $0
784	Isoniazid chemotherapy for low risk White male tuberculin reactors age 55	$17,000
Venous thromboembolism prevention		
230	Heparin (vs. anticoagulants) to prevent venous thromboembolism	≤ $0
769	Compression stockings to prevent venous thromboembolism	≤ $0
770	Compression stockings to prevent venous thromboembolism	≤ $0
770	Heparin to prevent venous thromboembolism	≤ $0
770	Heparin and dihydroergotamine to prevent venous thromboembolism	≤ $0
770	Intermittent pneumatic compression to prevent venous thromboembolism	≤ $0
770	Heparin and stockings to prevent venous thromboembolism	≤ $0
770	Warfarin sodium to prevent venous thromboembolism	≤ $0
769	Intermittent pneumatic compression and stockings to prevent thromboembolism	$400
230	Dextran (vs. anticoagulants) to prevent venous thromboembolism	$640
769	Heparin to prevent venous thromboembolism	$960
769	Heparin and stockings to prevent venous thromboembolism	$1,000
769	Heparin and dihydroergotamine to prevent venous thromboembolism	$1,700
769	Intermittent pneumatic compression to prevent venous thromboembolism	$2,400
787	Heparin, 1 day, for women with prosthetic heart valves undergoing surgery	$5,100
769	Heparin/dihydroergotamine (vs. stockings) to prevent venous thromboembolism	$42,000
787	Heparin, 3 days, for women with prosthetic heart valves undergoing surgery	$4,300,000
Medicine miscellaneous		
443	Broad-spectrum chemotherapy for cancer of unknown primary origin	≤ $0
728	Cefoxitin/gentamicin (vs. ceftizoxime) for intra-abdominal infection	$880
728	Mezlocillin/gentamicin (vs. ceftizoxime) for hospital acquired pneumonia	$1,400
646	Computed tomography in patients with severe headache	$4,800
709	Continuous (vs. nocturnal) oxygen for hypoxemic obstructive lung disease	$7,000
906	Preoperative chest X-ray to detect abnormalities in children	$360,000

[a] Reference numbers correspond to records in the database and to the references listed in Appendix B.

[b] Due to space limitations, life-saving interventions are described only briefly. When the original author compared the intervention to a baseline of "the status quo" or "do nothing" the baseline intervention is omitted here. Other baseline interventions appear as "(vs.)." Cost-effectiveness estimates are based on the particular life-saving intervention, base case intervention, target population, data, and methods as detailed by the original author(s). It is suggested the reader review the original document to gain a full appreciation of the origination of the estimates.

[c] All costs are in 1993 U.S. dollars and were updated with the general consumer price index. To emphasize the approximate nature of estimates, they are rounded to two significant figures.

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[a] Reference numbers correspond to records in the database and to interventions described in Appendix A. Missing numbers reflect documents that were retrieved but did not contain suitable cost-effectiveness data.

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EDITORIAL

The Cost-Effectiveness of Environmental Regulations Questioned

Steven Garry, CHP

In the last issue of the *Newsletter*, Gen Roessler wrote an editorial on the apparent communication failure between the health physics technocrats and the journalist Michael Fumento. As you may recall, Mr. Fumento wrote an article in *The Washington Times* which centered around the conclusions drawn from the two radon-risk studies (one on home radon and one on radon in mines). According to Fumento, the NCI/Lubin paper on miners "concludes by saying this appears to support the EPA position that 15,000 American lung-cancer deaths a year are from exposure to radon not in mines but in houses." The way I read Fumento's article, he was skeptical about the motivation for the conclusions drawn from the radon study of miners. Basically, Mr. Fumento made the supposition that "confusion may be the whole purpose of the most recent radon report (on radon in mines)."

I don't believe that this is an example of a communication failure between the technical health physicists and the non-technical journalists. Rather this is the case of a quite astute journalist who is focusing in on the public interest in Congressional action on "zeroing out of the budget." Evidently, Fumento believes that there is a possibility that EPA's Radon Action Program was being targeted for elimination in the Republican-dominated Congress. The case in point was the EPA defending its cause and role in spite of evidence to the contrary as expressed by a "huge number of epidemiologists, doctors, and physicists" who don't believe in the linear, no-threshold theory. This lack of support for the linear, no-threshold theory was further evidenced in the June 1995 issue of the HPS *Newsletter*, which supported Fumento's skepticism by stating the opinion of "radon-studying professionals" who "virtually all refute the no-threshold view" and that this is opposed to the view of "EPA and the radon establishment."

Mr. Fumento concludes his article by stating that there are even bigger ramifications to EPA than the potential loss of its radon program. This is the challenge to EPA's fundamental justification for environmental regulation, the assumption that environmental regulation is needed because cancer causation occurs at very low levels without a threshold.

The underlying issue in this story is an issue which both industry health physicists and governmental agencies are already working on, i.e., the cost-effectiveness of environmental regulations. Recent examples include a presentation at the USNRC Regulatory Information Conference (9 May 1995) by Dr. Gail de Planque, NRC Commissioner, titled "Risk Analysis and the Return to Common Sense." Similarly, the cost-effectiveness of proposed site cleanup standards is being debated in ongoing NRC rulemaking on the Radiological Criteria for Decommissioning. An issue being addressed is, is it worth millions of dollars to reduce the potential man-made exposure by a few mrem for the benefit of a few individuals who hypothetically might receive this exposure?

Several months ago Bill Mills, during his President-Elect chapter tours, told me about and later gave me a copy of an article published in the *Risk Analysis* Journal (Tengs et al.

[see EDITORIAL, page 4]

[EDITORIAL, continued from page 2]
1995). The introduction states, "Risk analysts have long been interested in strategies that can reduce mortality risks at reasonable cost to the public. Based on anecdotal and selective comparisons, analysts have noted that the cost-effectiveness of risk-reduction opportunities varies enormously, often over several orders of magnitude. Questions have been raised about whether it makes sense to spend millions of dollars per year of life saved on program X when program Y costs only thousands of dollars per year of life saved."

The basis for the cost/benefit study of life-saving interventions was researched by using publicly available economic analyses. Life-saving interventions were defined as any behavioral and/or technological strategy that reduced the probability of premature death. Cost-effectiveness was defined as the net resource costs of an intervention per life year saved (LYS). Costs were "direct," indirect costs were excluded. Costs and effectiveness were "net." At the low end, there were those interventions "that saved more resources than they consume (e.g., quit smoking), to those costing more than 10 billion dollars per year of life saved. The median intervention described in the literature costs $42,000 per life-year saved (n=587). Not only does variation over 11 orders of magnitude exist overall, it also exists within each category . . . "

The article continues "the median intervention in the transportation sector costs $56,000/life-year saved (n=87), while the median intervention in the occupational sector costs $346,000/life-year (n=36). Further dividing occupational interventions into those that avert fatal injuries and those that involve the control of toxins reveals medians of $68,000/life-year (n=16) and $1,388,000/life-year (n=20), respectively." Table 1 of the article lists the median costs of intervention by sector as follows: health care $19,000/LYS, residential $36,000/LYS, transportation $56,000/LYS, occupational $346,000/LYS, and environmental a whopping $4,207,000/LYS.

The article continues "the median-effectiveness of those governmental regulations for which we have data also varies considerably (see Table III). While the median Consumer Product Safety Commission (CPSC) rule costs $68,000/life-year saved (n=11), the median Environmental Protection Agency (EPA) rule costs more than 100 times more, or $7,629,000/life year saved (n=89)." Table III lists costs by regulatory agency: FAA as $23,000/LYS, CPSC $68,000/LYS, National Highway Traffic Safety Administration $78,000/ LYS, OSHA $88,000/LYS, and EPA $7,629,000/LYS. Table VI provides the "Ten Most Expensive Interventions," which include radionuclide emission control at NRC-licensed and non-DOE facilities as $2,612,903,000/LYS. Appendix C lists the cost/LYS by each of the two separate and independent researchers. Radionuclide emission control at nuclear power plants is listed as $103,598,095/LYS and $183,282,733/LYS. ALARA at nuclear power plants is $1,061,756/LYS and $2,500,549/LYS. Radionuclide emission control at uranium fuel cycle facilities was listed as $33,750,000,000/LYS. Radon control was listed in Table IV as $141,000/LYS.

I presume that the environmental regulation costs are based on a theoretical life-year lost. Note that some of the sectors and interventions deal with observable life loss; e.g., airplane and auto fatalities, whereas the environmental carcinogen causation of life loss is theoretical life loss, dependent upon the validity of the linear, no-threshold theory.

Let's compare this range of values for environmental regulations for manmade radiation, i.e., one hundred million to two billion dollars/LYS to the values that the public is willing to spend on its own care out of its own pocket. Values for what the public will spend are listed in the Health Physics Society "Position Statement on Radiation Dose Limits for the General Public, Part II" (published in the back of the membership handbook). The values determined are $5-$10 per statistical day of life. This is roughly $2,000-$4,000 per year, or approximately five orders of magnitude less than what the government is spending through environmental regulations on care of its own citizens.

In summary, I think we are putting too much attention on the wrong issue, the validity of the linear, no-threshold theory at low doses (most of us agree its in the range from zero to very small). Instead, in this era of "zeroing out the budget," health physicists should become more aware of the paradox risk analysts have identified, and become more concerned about reducing the cost ineffectiveness of environmental regulations.

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Tengs, Tammy O.; Adams, Miriam E.; Pliskin, Joseph S.; Safran, Dana Gelb; Siegel, Joanna E.; Weinstein, Milton C.; Graham, John D. Five-hundred life-saving interventions and their cost-effectiveness. Risk Analysis. 15(3): 369; 1995. ■

"We don't know the answer yet, but we're really getting off on the attention."

Appendix 2

Paper

TEST OF THE LINEAR-NO THRESHOLD THEORY OF RADIATION CARCINOGENESIS FOR INHALED RADON DECAY PRODUCTS

Bernard L. Cohen*

Abstract—Data on lung cancer mortality rates vs. average radon concentration in homes for 1,601 U.S. counties are used to test the linear-no threshold theory. The widely recognized problems with ecological studies, as applied to this work, are addressed extensively. With or without corrections for variations in smoking prevalence, there is a strong tendency for lung cancer rates to decrease with increasing radon exposure, in sharp contrast to the increase expected from the theory. The discrepancy in slope is about 20 standard deviations. It is shown that uncertainties in lung cancer rates, radon exposures, and smoking prevalence are not important and that confounding by 54 socioeconomic factors, by geography, and by altitude and climate can explain only a small fraction of the discrepancy. Effects of known radon-smoking prevalence correlations—rural people have higher radon levels and smoke less than urban people, and smokers are exposed to less radon than non-smokers—are calculated and found to be trivial. In spite of extensive efforts, no potential explanation for the discrepancy other than failure of the linear-no threshold theory for carcinogenesis from inhaled radon decay products could be found.

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Key words: radon; carcinogenesis; lungs, human; radiation, low-level

INTRODUCTION

THE CANCER risk from low level radiation is normally estimated by use of a linear-no threshold theory (with or without added terms that apply at higher doses). This theory is a logical consequence of the widely accepted view that a single particle of radiation interacting with a single cell nucleus can initiate a cancer; the number of initiating events is then obviously proportional to the number of particles of radiation, and hence to the dose. However, there is nothing in this line of reasoning about the role of biological defense mechanisms that prevent the billions of potential initiating events we all experience from each developing into a fatal cancer. If exposure to low level radiation were to stimulate these biological defense mechanisms, that effect would be added to the effect of linear-no threshold, and could cause a radical deviation of observed effects from the predictions of that theory alone in the low dose region.

There is now a substantial body of evidence indicating that low level radiation does indeed stimulate such biological defense mechanisms (Luckey 1991; Sugahara et al. 1992; Calabrese 1994). For example, it has been shown (Shadley and Wolfe 1987) that human lymphocyte cells previously exposed to low level radiation suffer fewer chromatid breaks when later exposed to large radiation doses, and this effect has been traced to stimulated production of repair enzymes by the low level radiation (Wolfe 1992). Similar effects have been demonstrated *in vivo* for bone marrow cells and spermatocytes in mice (Cai and Liu 1990). In addition to reducing chromosome aberrations, pre-exposure to low level radiation has been found to reduce induction of mutations (Sanderson and Morely 1986; Kelsey et al. 1991) and to increase survival rates (Shadley and Dai 1992; Azzam et al. 1992) in cells later exposed to high radiation doses. Low dose pre-exposure of drosophila reduces the number of dominant lethal mutations induced by later high dose radiation (Fritz-Niggli and Schaeppi-Buechi 1991). Low dose radiation has also been shown to stimulate immune functions in mice as measured by PFC (plaque-forming cell) reaction, MLC reaction (mixed lymphocyte culture, used as a test for T-cell function), reaction to Con A (concanavalin-A, a lectin that stimulates T-lymphocytes), NK (natural killer cells, which recognize and kill tumor cells) activity, and ADCC activity (anti-body dependent cell mediated cytotoxicity, which assists NK activity) in splenocytes (Liu 1992).

All of this evidence surely leaves linear-no threshold open to serious question in its applications to low level radiation. These applications have had tremendous societal consequences—adding over 100 billion dollars to the cost of U.S. nuclear power plants and largely denying the nation the great potential benefits of that technology, leading to expenditure of a projected 150 billion dollars for clean-up of government facilities, etc.—all this in spite of the fact that linear-no

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threshold theory has never been verified with experimental data in the low dose, low dose rate region of all the important applications. Clearly, then, it is of utmost importance to further seek such verification. That is the purpose of this paper.

LUNG CANCER RATES VS. INDOOR RADON LEVELS

A compilation has recently been completed of average indoor radon levels in 1,729 U.S. counties, over half of all U.S. counties and representing nearly 90% of the total U.S. population (Cohen 1992, 1994). Data from it were used to derive Fig. 1 (a and b) which show plots of age-adjusted lung cancer mortality rates, m, for white males (1a) and females (1b) (Riggan and Mason 1983) vs. average radon level, r, in living areas of homes in these counties. Radon levels are given in the widely used units of $r_0 = 37$ Bq m^{-3} (1.0 pCi L^{-1}). Rather than showing a data point for each county, all counties within various ranges of r (marked on the base line) are grouped together, and only the average m for each group is plotted, along with the standard deviation of the mean (error bars) and the first and third quartiles. The solid line is the best straight line fit to the data for the individual counties. In Fig. 1 (a and b), we see a clear tendency for m to decrease with increasing r, in sharp contrast to the increase expected from the fact that radon is believed to cause lung cancer.

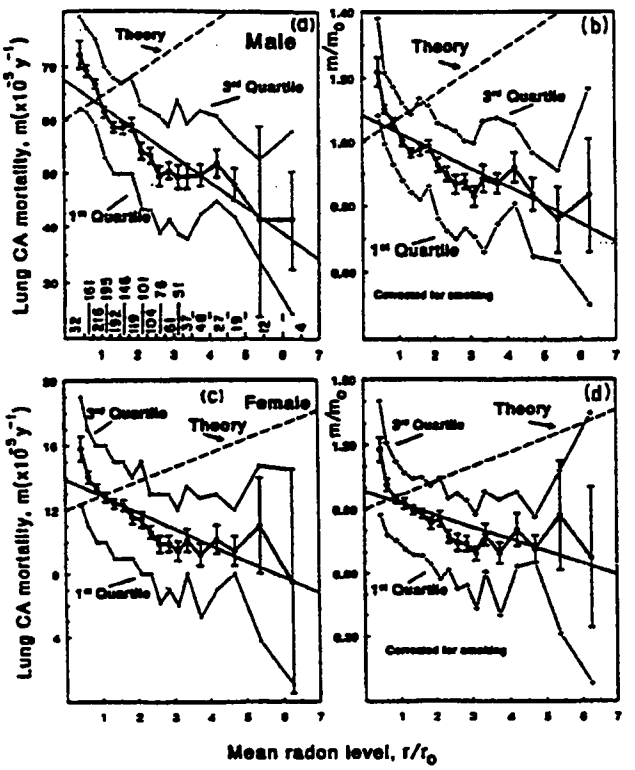

Fig. 1. Lung cancer mortality rates vs. mean radon level for 1,601 U.S. counties. Data points shown are average of ordinates for all counties within the range of r-values shown on the baseline of Fig. 1a; the number of counties within that range is also shown there. Error bars are standard deviation of the mean, and the first and third quartiles of the distributions are also shown. Fig. 1c, d are lung cancer rates corrected for smoking prevalence (m/m_0) vs. radon level [eqns (5) and (6)]. Theory lines are arbitrarily normalized lines increasing at a rate of 7.3%/r_0.

These data, although they are potentially explainable in many ways, are the starting point of a test of the linear-no threshold theory. A preliminary report of this test (based on data for 965 counties from a single data source) has been published previously (Cohen and Colditz 1994). There have been about 50 studies of the relationship between radon exposure and lung cancer reviewed recently by Neuberger (1991, 1992). Of these, 13 have involved measurements of radon levels including 7 ecological studies, 4 case-control studies, and 2 that involve both. A later report on one of the studies has appeared recently (Schoenberg 1992) and at least one ecological study was not included in the review (Haynes 1988). A recent review (Stidley and Samet 1993) discusses problems with these ecological studies. There have been two recent case-control studies (Perslagen 1994; Letourneau 1994) that have attracted substantial attention but neither of these gives useful information in the region below 5_{r_0} where essentially all data in Fig. 1 are contained.

A. The ecological fallacy

Fig. 1 is an example of what epidemiologists call an "ecological study," which means that it compares the average mortality rates for groups of people (i.e., populations of counties), m, with their average exposure, r. This is quite different from what epidemiologists normally study, the mortality risk to an individual, m', vs. that individual's exposure to radon, r'. To illustrate the difference, let us suppose that only radon levels above 20 r_0 can cause cancer, and that county X has $r = 1.5\ r_0$ but no exposures above 20 r_0 while county Y has $r = 1.0\ r_0$ but 1% of its population is exposed above 20 r_0; then county Y would have the higher cancer rate, m, even though county X has the higher average radon exposure, r. To state the problem succinctly, the average exposure does not determine the average risk. This is the major contributor to what is called "the ecological fallacy" (Robinson 1950; Selvin 1958).

However, it has been shown (Cohen 1990a, 1990b) that the above problem does not apply when there is a linear-no threshold relationship. This is familiar to health physicists from the well known fact that "person-rem," an ecological quantity, determines the number of deaths in a cohort, regardless of how the dose is distributed among the individuals in the cohort. Expressing this loosely in terms of our problem, the cohort is the population of a county; dividing the number of deaths by the population gives the mortality rate, m, and dividing person-rem by the population gives the average exposure, r. This indicates crudely

why m vs. r data like those shown in Fig. 1 are not affected by the above problem. A more complete demonstration is given in the next section, and it is refined through the rest of the paper.

Other problems arising from the fact that this is an ecological study, often called "ecological bias," will be discussed in section P.

B. Smoking prevalence, S

An obvious potential explanation for the unexpected pattern of Fig. 1 (a and b) is that there may be a strong tendency for the prevalence of cigarette smoking, S, to be higher in low radon counties than in high radon counties; that is, there is a large negative r-S correlation.

The effect of smoking prevalence is most conveniently treated by use of the BEIR IV theory (NAS 1988), which gives separate risk estimates for smokers and non-smokers. First let us consider non-smokers only, for which we use the subscript n. According to BEIR IV, the mortality risk for individual i, m_i, of age A_i, living in a house with radon level r_i, in a given year is

$$m_i' = a_n g(A_i)[1 + h(A_i) r_i'] \qquad (1)$$

where g and h are given in BEIR IV as a function of age, and a_n is a constant inserted here for convenience in normalizing.

We next sum both sides of eqn (1) over i and divide by the number of individuals in the cohort, q. The sum over m_i' gives the total number of deaths among non-smokers, and dividing this by q gives the mortality rate from lung cancer among non-smokers, m_n. The sum over the right side of eqn (1) is evaluated in Appendix A. Dividing that result by q and equating it to m_n then gives

$$m_n = a_n (1 + br) \qquad (2)$$

where $b = 10.8\%/r_0$.

We now turn to consider smokers. Let p = the number of smokers in the county and we repeat the above process for smokers to obtain analogously

$$m_s = a_s (1 + br).$$

Note that we assume here that the average radon level, r, is the same in houses of smokers and non-smokers; this assumption is relaxed in section L. Note also that, as discussed in Appendix A, the constant b is the same for smokers and non-smokers; this assumption is peculiar to the BEIR IV model and it is relaxed in section M.

The total lung cancer mortality rate for the county, including the number of deaths among smokers, $p\,m_s$, and among non- smokers, $q\,m_n$, with their sum divided by the total population of the county, $(p + q)$, is

$$m = (pm_s + qm_n)/(p + q).$$

In terms of the smoking prevalence, $S = p/(p+q)$, this reduces to

$$m = [Sa_s + (1 - S)a_n] (1 + br) \qquad (3)$$

C. Migration

One obvious problem in our test is that people move frequently and therefore do not spend their whole lives—and receive all of their radon exposure—in their county of residence at time of death, where their death is recorded and contributes to mortality rates. This problem has been treated in some detail previously (Cohen 1990b, 1992a, 1993); the procedure selected was to assume that people spend a fraction of their lives, f, in their county of residence at death, and the remaining fraction, $(1 - f)$, in areas of U.S. average radon level, $\bar{r}$. With the exception of Florida (FL), California (CA), and Arizona (AZ), where many people move to retire, all areas of the U.S. have $f > 0.5$, and the national average is $f = 0.7$ (Cohen 1992a). The three retirement states (FL, CA, AZ) were deleted from the study, reducing the total number of counties to 1,601. (This has no significant effect on the results of the analyses that follow.) Eqn (3) is modified by the assumption to

$$m = [Sa_s + (1 - S)a_n](1 + 0.3b\bar{r} + 0.7br) \qquad (4)$$

The migration problem is thereby handled to a reasonable approximation by modifying the theory, and no correction to the data is necessary. Dividing both sides of eqn (4) by $[Sa_s + (1-S)a_n]$ $(1+0.3\bar{r})$ and inserting the BEIR IV values of the constants (Cohen and Colditz 1994) converts this to

$$m/m_0 = 1 + Br \qquad (5)$$

where $B = 7.3$

$$\begin{aligned} m_0 &= (9 + 99S) \quad \text{males} \\ m_0 &= (3.7 + 32S) \quad \text{females,} \end{aligned} \qquad (5a)$$

where B is in units of $\%/r_0$ [$\%/37$ Bq m^{-3} ($\%$/pCi L^{-1})] and m_0 is in units of deaths y^{-1} per 100,000 population. In order to compare data with theory, one should, therefore, plot m/m_0 vs. r. Such plots are shown in Fig. 1 (c and d); the methodology for estimating S to determine m_0 for each county is given in Cohen and Colditz (1994) and will be discussed further below (section G). Fig. 1 (c and d) may be viewed as Fig. 1 (a and b) corrected for variations in smoking prevalence. Note that correcting for smoking does little to explain the unexpected behavior of the data.

Further discussion considers plots of m/m_0 vs. r (like those in Fig. 1c and 1d), concentrating on the slope, B; BEIR IV theory predicts $B = +7.3$ (eqn 5a). For comparison with observations, the best fit of the data to

$$m/m_0 = A + Br \qquad (6)$$

is used to derive values of A and B. One might use B/A in eqn (6) as the quantity to be compared with B in eqn (5), but this would be equivalent to normalizing the line through the data to the theory line at $r = 0$. However, it would be more appropriate to normalize these lines in the region where most of the data points

lie, at about $1.2\,r_0$ (Fig. 1), which is crudely equivalent to using $B/0.9A$. To simplify the problem, B-values from eqns (6) and (5) are compared directly, ignoring the small differences between $0.9A$ and 1.00 (typically < 10%).

The best fits to the data points for the 1,601 counties in Fig. 1 (c and d) give $B = -7.3 \pm 0.6$ for males (± is one standard error) and $B = -8.3 \pm 0.8$ for females, discrepant by about 20 standard deviations with the values expected from BEIR IV theory, $B = +7.3$. This difference will be called "the discrepancy," and the remainder of this paper deals with the attempts to explain it. If data from Florida, California, and Arizona were not deleted, results would be $B = -6.5 \pm 0.7$ for males and $B = -9.0 \pm 0.8$ for females.

It is immediately clear that the discrepancy cannot be explained by statistics; the probability for chance discrepancies of 20 standard errors is truly negligible.

D. Uncertainties in radon data

The compilation of radon data used here derives from three independent sources:

- University of Pittsburgh measurements (PITT);
- Measurements by U.S. Environmental Protection Agency (EPA); and
- Data bases compiled by individual states, not based on PITT or EPA (STATE).

The data used in Fig. 1, TOTAL, is an average of as many of these three as are available for each county. The evidence for the reliability of these data has been discussed extensively (Cohen 1992c,1994b).

The results for B from the various data sets treated separately are

DataSet	*Counties*	*B(male)*	*B(female)*
PITT	1,151	−6.4	−9.1
EPA	1,074	−6.4	−6.3
STATE	358	−6.8	−10.8

as compared with $B = -7.3$ for males and $B = -8.3$ for females from TOTAL. For the 663 counties included in both PITT and EPA, the results for B are

PITT	663	−5.8	−7.3
EPA	663	−5.5	−6.7

For the 296 counties in both PITT and STATE, the results for B are

PITT	296	−6.4	−13.4
STATE	296	−6.3	−12.1

Note that each of the independent data sets gives essentially the same result, especially when an identical selection of counties is used. This gives a high degree of confidence that errors in the values of r are not responsible for the discrepancy, or for any significant fraction of it.

By studying correlations between values of r for specific counties from the separate data sources, estimates of uncertainties in the individual r-values were derived (Cohen 1992c). They are generally about 17% (one standard error). If these uncertainties are random in direction—and it is difficult to imagine reasons why they might be otherwise—this should bias our values of B toward the null by about 17% (Fuller 1987). For example, the B value for males should be corrected for this bias from −7.3 to −8.5, further increasing the discrepancy. This correction will not be used in the following discussion, but it would easily compensate for most of the small corrections to be considered later that might reduce the negative value of B.

One problem common to PITT, EPA, and STATE is that people who live in apartment buildings, where radon levels are generally low, are under-represented. To investigate this problem, data are available on H5, the percentage of housing units that are in buildings containing 5 or more units (U.S. Census 1982). An extreme correction for this problem would be to assume that none of these are included in the radon surveys and that all of them have zero radon concentrations. This correction changes B from −7.3 to −7.1 for males, and from −8.3 to −8.4 for females.

Another approach to this problem is to delete the counties with large H5. If the 20% with the largest H5 were deleted (H5 > 16.6%), B would be changed to −7.2 for males and −7.9 for females. If the 40% with the largest H5 were deleted (H5 > 8.9%), B-values would become −6.7 and −6.7, respectively. If the 60% with the largest H5 were deleted (H5 > 5.7%), B-values would be −6.2 and −7.3, respectively. It thus seems clear that the "apartment problem" is not an important cause of the discrepancy.

The slope of a regression line can often be heavily and unduly influenced by the effects of a few outlying data points. To investigate this effect, various indices suggested in the statistics literature were used for discarding 10 and 20 outliers—leverages (L), studentized residuals (S), Cook's distance (C), DFITS (D), and residuals (R) in the regression of m/m_0 vs. r. The results for the slope, B, are listed in Table 1. In all cases, discarding outliers increases the negative value of B, making the discrepancy worse. Outliers were not discarded in further analyses.

Table 1. Effects of discarding outliers. These are values of B obtained if 10 or 20 counties are discarded on the basis of various indices: L (leverages), S (studentized residuals), C (Cook's distance), D (DFITS), and R (residuals).

	Discard 10		Discard 20	
Index	Male	Female	Male	Female
L	−7.8	−8.7	−7.7	−9.3
S	−7.7	−8.9	−7.6	−9.3
C	−7.3	−9.1	−7.7	−9.1
D	−7.8	−9.4	−8.3	−10.0
R	−7.8	−8.9	−7.7	−9.3

An unrelated problem with the accuracy of the r-values derives from the number of measurements on which they are based. It is shown at the end of section H that this does not affect the results.

E. Sampling issues

One might wonder whether the discrepancy can be explained by peculiarities in the sample of U.S. counties under study. One way to test this is to break the data into subsets and determine B independently for each subset. Table 2 shows the results for 10 randomly selected subsets each of 800, 400, and 200 counties. The results are always reasonably close to those for the entire data set, $B = -7.3$ for males and -8.3 for females. Even a study of 200 counties would clearly show the discrepancy. In that sense, this work might be considered as eight separate studies, each leading to the same conclusion.

Dividing the data into subsets on bases other than random selection will be discussed later in this paper but again the discrepancy is invariably encountered.

One might wonder how unexpected it is to find such a large and statistically robust correlation between m and r as we find for lung cancer even if there is no causal explanation for it. In a separate project, regressions of m on r, and of m on r and S, for 33 different cancer sites were studied (Cohen 1993). Whether or not S is included, the number of standard deviations by which B differs from zero, and the coefficient of determination, R^2, were found to be at least 2.7 times larger for lung cancer than for any other cancer type, and for all but two types they were at least 4 times larger. One must therefore conclude that the strong m-r correlation seen in Fig. 1 is a truly unusual and remarkable occurrence, and therefore should not be dismissed as something that might occur by chance with reasonable probability.

F. Uncertainties in lung cancer mortality rates, M

Lung cancer mortality rates (Riggan and Mason 1983) are derived from mortality records for 1970–1979 which are the latest age-adjusted rates available at this time [Cohen and Colditz (1994) presents a crude analysis using more recent data; it makes the discrepancy larger]. No attempt was made to analyze uncertainties arising from variations in the efficiency of collecting these data, but it is difficult to imagine reasons why these variations might correlate with radon levels other than through geography as a confounder, a topic treated later in this paper.

Table 2. Values of B derived from 10 randomly selected subsets of 800, 400, and 200 counties. Bottom row is the standard deviation of the mean, determined from the 10 values listed.

	Males			Females		
Select No.	800	400	200	800	400	200
1	−6.9	−6.5	−5.8	−6.7	−5.4	−4.8
2	−7.6	−7.8	−7.8	−7.8	−6.8	−6.5
3	−7.8	−6.9	−7.0	−7.5	−8.9	−10.7
4	−7.2	−7.9	−8.3	−7.4	−10.5	−9.2
5	−7.1	−6.4	−5.6	−10.1	−10.9	−10.0
6	−7.8	−8.0	−7.0	−6.9	−5.4	−4.2
7	−6.2	−5.8	−5.5	−8.1	−9.0	−8.0
8	−6.9	−7.8	−5.0	−8.4	−6.4	−6.6
9	−7.3	−6.4	−7.1	−10.1	−10.3	−12.7
10	−8.7	−10.9	−8.5	−9.9	−9.6	−11.9
Average	−7.4	−7.4	−6.8	−8.3	−8.3	−8.5
SD	0.2	0.4	0.4	0.4	0.7	0.9

One problem that can be treated is that arising from statistical uncertainties; low population counties had relatively few lung cancer deaths in 1970–1979. The distributions of lung cancer mortality rates, m, for all counties within a narrow range of radon levels have typical relative standard deviations of 24% for males and 34% for females. If the statistical uncertainty for m is no more than half this large, its statistical accuracy may be judged to be irrelevant; this requires at least 69 deaths for males and 35 deaths for females, which are roughly the numbers expected in counties with populations of 23,000 and 58,000, respectively.

As a test of this problem, all counties with at least these populations were given equal weight, while counties with lower populations were given weights inversely proportional to the variance of m, which is just proportional to their population. With this criterion, weights are reduced for 465 of the 1,601 counties for males, and for 994 counties for females. When this weighting was used in the regression of m/m_0 vs. r to determine the slope B, the values of B were changed from -7.3 ± 0.6 to -7.1 ± 0.5 for males and from -8.3 ± 0.8 to -7.4 ± 0.7 for females. Since these changes are relatively small, this weighting was not used in our other studies.

G. Uncertainties in smoking prevalence, S

Direct information on smoking prevalence is available only by state, with the best data derived from a 1985 survey by Bureau of Census (U.S. PHS 1990). This was corrected to the appropriate time period for deaths occurring in 1970–1979 by use of data on the time variation of the national smoking prevalence (U.S. PHS 1987) assuming that the relative prevalence for each state remained unchanged. This gives the smoking prevalence for each state, S'. It was then assumed that the S-value for a county was S' times a correction factor for the fraction of the county population that lives in an urban area, PU; this correction factor was derived from a regression of lung cancer rates on PU and was found to be remarkably constant for all regions of the nation.

This procedure gives a distribution of S-values within a single state about half as wide as the distribution of S-values for the various states. To investigate suggestions that this may seriously underrepresent the variations of S for counties within a state, the above correction factor was doubled in magnitude; this changed B from −7.3 to −7.0 for males and from −8.3 to −8.0 for females, a trivial effect.

There are three obvious problems in this method of deriving S-values:

(a) The direct data are derived from a 1985 survey, which is inappropriate for predicting lung cancer mortality in 1970–1979.
(b) The direct data are on smoking prevalence in states rather than in counties.
(c) There is no consideration of intensity of smoking, degree of inhalation, use of filters, etc.

Problem (a) and part of problem (c) can be avoided if we derive S' values from state cigarette sales tax collections, which are available on a yearly basis (Tobacco Institute 1988). If these are taken to be proportional to S' for males, and the method outlined above is used to derive S-values, the results are

- 1975: $B = -8.3 \pm 0.7$;
- 1970: $B = -9.0 \pm 0.6$; and
- 1960: $B = -10.1 \pm 0.7$.

The discrepancy is larger for this source of data than for that used in Fig. 1 ($B = -7.3$). This source was not used in the other studies.

An alternative approach for deriving S-values that avoids all three of the above problems is to use lung cancer rates in counties. This, of course, must be done in a way that is independent of r, which is accomplished by stratifying the data on the basis of radon levels, r, into six subsets. All counties in a given subset therefore have approximately the same r-value.

Since variations in S are principally due to socioeconomic factors, values of S for each county are estimated from a linear combination of socioeconomic variables (SEV). The 54 SEV available for each county that are used here and in later parts of our analysis are listed in Appendix B; they are basically all of those in County and City Data Book—1988 (U.S. Census 1988) that are not intrinsically proportional to population, plus a few others, including population and population density. The original S' is also included as an SEV. A scoring system was then developed to determine which of these SEVs are most useful for predicting m for each of the six subsets of counties. Out of a possible 384 points, the highest scores for males were S': 369; HA: 295; PU: 164; EW: 123; GR: 107; and SC: 99 (no others were > 69). The highest scores for females were S': 319; EF: 227; SC: 146; GR: 125; PT: 118; EW: 103; and PU: 101 (no others were > 94).

Multiple regressions of m on these SEV were done for each of the six subsets, and coefficients for each SEV were recorded. In all but one case (GR for females, which was therefore not used), these coefficients were reasonably consistent among the subsets, and average coefficients were derived. These average coefficients were then used to determine S-values for each county from values of its SEV. Note that these S-values do not suffer from any of the problems, (a), (b), (c), listed above. When these S-values are used in eqn (5a) to determine m_0 for use in eqn (6), negative B-values are reduced from -7.3 to -6.0 for males and from $B = -8.3$ to -6.3 for females. They thus give only a minor reduction in our discrepancy.

Since using m-values to determine a parameter, S, to be used in fitting m-values is a somewhat questionable procedure, the original S-values were used for further studies. However, this exercise gives confidence that problems (a), (b), (c) listed above are not responsible for much of the discrepancy.

Nevertheless, the values of S being used are subject to substantial uncertainty, leaving open the possibility that errors in S can somehow explain the discrepancy. This would be the case if the true S-values had a much stronger negative r-S correlation than those being used. To quantify this potential effect, the S-values for the 1,601 counties were reassigned in perfect reverse order of their r-values. This "perfect" negative r-S correlation gives a coefficient of correlation (CORR) between r and S of -0.96 for males and -0.92 for females. When these reassigned S-values are used in eqn (5a) to calculate m_0 for use in eqn (6), the results are $B = +0.7$ for males and $B = -0.3$ for females. The negative slopes are eliminated but only about half of the discrepancy is explained; these B-values are far short of $+7.3$ expected from theory.

While this perfect negative r-S correlation is a drastic assumption, one can go even further and broaden the distribution of S-values for the 1,601 counties. The characteristics of this distribution for males (S in percent) are as follows: mean = 51.7; standard deviation (SD) = 6.9; and min/max = 25.5/69.8. As a broadened distribution, the S-value for each county is taken to be twice as different from the mean. This gives a distribution with mean = 51.7; SD = 13.8; and min/max = 0/88. These S-values are then reassigned to counties in perfect reverse order of their r-values to obtain a "perfect" negative r-S correlation—S(perfect)—as before: alternatively these S-values are reassigned to counties randomly to obtain S (random). S is then taken to be

$$S = G\,S(\text{perfect}) + (1 - G)\,S(\text{random}),$$

where G is a parameter that can be varied to obtain any desired negative coefficient of correlation (CORR-r) between S and r. To eliminate the negative slope in Fig. 1 (i.e. to make $B = 0$) is found to require CORR-$r = -0.64$, and to obtain the theory value, $B = +7.3$, requires CORR-$r = -0.90$. Recall that these results are based on the drastic assumption that the width of the distribution of S-values is twice as large as in the best estimates. An analysis which is independent of the width of the distribution of S-values is presented at the end of section M.

If one is completely skeptical about the methods used here to estimate S-values, an alternative approach is to assume that the distribution of S-values is the same as the distribution of lung cancer mortality rates, m, for males (aside from a normalizing factor to

give the correct national average for S), and calculate the CORR-r required to explain the discrepancy. This would seem to give an upper limit on the width of the S-distribution since other factors must contribute to the width of the m-distribution. Utilizing the methods of the previous paragraph—combining S(perfect) and S(random) in various ratios—it is found that obtaining the theory value, $B = +7.3$, requires CORR-$r = -0.91$, and just eliminating the negative slope to make $B = 0$ requires CORR-$r = -0.62$.

Consideration was next given to the likelihood of such strong r-S correlations. Since there is no apparent direct causal relationship between r and S, the most likely source of r-S correlations is confounding by socioeconomic variables, SEV. It therefore seems reasonable to expect the r-S correlation to be similar to the correlation of r with these SEV.

The largest magnitude correlation with r (|CORR-r|) for any of the 54 SEV is 0.37 for EF which is clearly an urban vs. rural effect which will be treated in detail in section L, and this effect may also explain all of the five largest |CORR-r|. The second largest |CORR-r| is 0.30, and for 49 of the 54 SEV it is less than 0.23. For the S-values being used here, CORR-$r = -0.28$ for males and -0.19 for females; for the S-values derived from cigarette sales tax data, CORR-$r = -0.16$ for 1975, -0.16 for 1970, and -0.11 for 1960. For the S-values derived from lung cancer rates, CORR-$r = -0.40$ for males and -0.34 for females.

From these examples, it seems clear that the negative r-S correlations cannot be nearly as strong as those needed to reduce B to zero, let alone to produce the large positive B predicted by the theory. It is therefore reasonable to conclude that uncertainties in S are not a very important cause of our discrepancy.

H. Confounding factors that correlate with socioeconomic variables (SEV)

If the theory is correct, the only reasonable explanation for the discrepancy is that there are one or more confounding factors that correlate strongly and with opposite signs with both m and r. They thereby introduce a strong negative correlation between m and r which is not due to a direct causal relationship. Smoking was the obvious candidate because of its known strong correlation with lung cancer, but it was considered in great detail above, and found not to explain the discrepancy. The next most obvious type of confounder would be socioeconomic variables (SEV). Consideration was therefore given to each of the 54 SEV listed in Appendix B as a possible confounding factor (CF).

If a particular SEV is an important CF, stratifying the data on it into subsets would greatly reduce the problem as each subset (i.e., each stratum) would have approximately the same value of the CF. The average of the B-values obtained from analysis of each of the various subsets would then give a value of B free from the effects of confounding.

The data are stratified into quintiles of 1,601/5 = 320 counties each, on the basis of each of the 54 SEV in turn. This gives 54 × 5 (quintiles) × 2 (sexes) = 540 subsets, each analyzed to derive a value of B. The results are shown in Table 3. Note there that all 540 B-values are negative. Thus, the negative slopes in Fig. 1 (c and d) are found if we consider only the most urban counties, or if we consider only the completely rural counties; if we consider only the richest counties or if we consider only the poorest; if we consider only those with the best medical care, or if we consider only those with the worst medical care; if we consider only the most rapidly growing counties or only the counties with declining populations; and so forth for each of the 54 SEV. These negative slopes are also found for all the strata in between, as for example, if we consider only counties with close to the national average income, or close to average education, or medical care, or any one of the other 51 SEV.

Averages over the five quintiles for each SEV and sex are shown in the last four columns of Table 3 along with their t-ratios, the number of standard deviations by which B differs from zero. The average value of B for the five quintiles, which is a determination of B free of confounding by that SEV, vary for males from -5.6 to -7.7 with a mean of -6.9 ± 0.5, and for females from -5.4 to -9.1 with a mean of -7.7 ± 0.8, quite close to the values for the entire data set, -7.3 and -8.3, respectively.

Thus, it is clear that no one of the SEV is an important enough CF to explain more than a tiny fraction of the discrepancy. Since SEV are normally strongly correlated with some other SEV, this probably means that no SEV is an important enough CF to substantially reduce the discrepancy. In fact, no factor which correlates strongly with any of the SEV can explain much of the discrepancy as that SEV would act as a surrogate for it in analyses like those done here. For example, air pollution cannot be an important CF since it correlates strongly with several of the SEV.

The last two rows of Table 3 show the results of stratifying on the number of radon measurements in the PITT and EPA data bases. The consistency of these results indicates that insufficient numbers of radon measurements in some counties is not an important source of difficulty.

I. Confounding by combinations of socioeconomic factors

Another possibility is that some combination of SEV may act cooperatively to confound the M-r relationship (where $M = m/m_0$). The best available approach to investigating this question is through multiple regression analysis, taking the relationship for each county to be

$$M = m/m_0 = A + Br + C_1X_1 + \ldots + C_{54}X_{54}, \quad (7)$$

where $X_1, X_2, \ldots, X_{54}$ are the values of the 54 SEV and A, B, $C_1, C_2, \ldots, C_{54}$ are the constants chosen to

Table 3. Values of B obtained from stratifying the data into quintiles ($Q_1, \ldots, Q_5$) on the basis of each of the SEV. Note from the column headings that minus signs and decimal points have been deleted to save space. The last four columns are averages of values for the five quintiles.

	−10B for males					−10B for females					Average male		Average female	
SEV	Q-1	Q-2	Q-3	Q-4	Q-5	Q-1	Q-2	Q-3	Q-4	Q-5	B	t	B	t
PT	63	74	65	44	55	105	54	44	32	87	−6.0	−4.9	−6.4	−3.8
PD	59	67	64	73	28	65	89	64	71	58	−5.8	−4.72	−6.9	−4.05
PI	51	69	46	85	116	97	102	65	74	39	−7.3	−6.04	−7.5	−4.29
PU	71	63	76	72	69	90	67	83	69	92	−7.0	−5.87	−8.0	−4.88
PW	74	54	55	47	49	73	18	66	35	83	−5.6	−3.67	−5.5	−2.65
PS	50	62	31	77	82	71	73	46	80	54	−6.0	−4.33	−6.5	−3.42
PE	94	47	51	72	92	57	21	73	85	136	−7.1	−5.89	−7.4	−4.26
PO	105	50	60	12	93	85	1	71	33	121	−6.4	−4.54	−6.2	−3.29
PY	81	71	46	38	132	109	100	115	44	24	−7.4	−6.05	−7.8	−4.84
PN	68	92	57	74	71	111	93	74	75	47	−7.2	−6.00	−8.0	−4.57
PH	67	81	57	45	127	93	104	102	24	76	−7.5	−6.25	−7.9	−4.69
VB	41	55	54	82	124	81	66	91	79	97	−7.1	−5.97	−8.3	−4.72
VC	85	50	25	68	66	106	100	40	65	67	−5.9	−4.71	−7.6	−4.04
VD	73	85	65	54	86	65	50	76	77	133	−7.3	−6.16	−8.0	−4.60
VI	56	66	48	88	96	77	93	49	70	98	−7.1	−5.83	−7.7	−4.33
VM	80	44	76	51	84	70	100	75	88	54	−6.7	−5.48	−7.7	−4.38
VS	74	78	49	64	57	102	101	76	11	28	−6.4	−5.29	−6.4	−3.52
VP	65	69	81	72	68	84	99	55	44	89	−7.1	−5.89	−7.4	−4.28
VH	81	79	59	51	93	38	100	76	71	136	−7.3	−6.05	−8.4	−5.05
SS	95	60	67	51	89	65	47	70	76	130	−7.2	−6.02	−7.8	−4.43
SC	83	40	62	72	81	69	97	39	74	81	−6.8	−5.65	−7.2	−4.05
SH	73	91	61	40	77	83	82	76	109	107	−6.8	−7.56	−9.1	−6.47
SU	64	50	98	69	84	69	75	80	96	99	−7.3	−6.09	−8.4	−4.73
SE	39	44	80	74	103	58	67	76	103	118	−6.8	−5.65	−8.4	−4.85
HO	78	85	46	51	113	91	79	58	81	86	−7.5	−6.07	−7.9	−4.53
HA	74	54	59	51	71	65	56	53	83	77	−6.2	−5.02	−6.7	−3.75
HV	98	49	50	73	90	47	83	107	85	99	−7.2	−6.01	−8.4	−4.87
HN	64	48	97	80	92	37	107	80	102	79	−7.6	−6.13	−8.1	−4.55
EI	79	88	66	61	70	73	91	95	58	82	−7.3	−6.13	−8.0	−4.56
EH	92	84	69	47	80	71	114	89	74	62	−7.4	−6.17	−8.2	−4.68
EJ	45	38	77	96	102	77	88	87	141	43	−7.2	−5.97	−8.7	−4.98
EV	45	44	65	105	102	86	92	69	143	52	−7.2	−5.96	−8.8	−5.08
EU	97	64	47	59	89	115	76	82	76	27	−7.1	−5.83	−7.5	−4.46
EW	59	81	59	55	76	95	63	72	62	42	−6.6	−5.39	−6.7	−3.76
EP	89	76	75	58	85	37	112	56	67	164	−7.7	−6.28	−8.7	−5.01
EM	78	87	76	66	14	91	148	129	36	13	−6.4	−5.34	−7.8	−4.67
ER	48	82	59	83	93	65	69	83	85	97	−7.3	−6.20	−8.0	−4.65
ES	74	64	68	73	79	64	71	80	86	97	−7.2	−6.09	−8.0	−4.76
EG	54	91	70	66	81	88	62	60	89	104	−7.2	−6.10	−8.1	−4.58
EF	75	53	70	55	48	64	83	34	13	75	−6.0	−4.77	−5.4	−3.01
EA	62	48	51	78	67	108	35	65	109	63	−6.1	−5.04	−7.6	−4.27
EL	68	92	80	61	43	100	144	92	61	29	−6.9	−5.64	−8.5	−4.83
ED	58	51	72	87	84	64	67	81	95	81	−7.0	−5.93	−7.8	−4.52
EC	77	72	61	67	82	91	84	75	44	106	−7.2	−6.19	−8.0	−4.74
EX	72	61	68	80	81	77	96	92	51	89	−7.2	−6.22	−8.1	−4.71
GF	74	32	94	80	81	55	28	70	132	107	−7.2	−6.04	−7.8	−4.44
GL	58	43	64	65	116	53	62	91	54	137	−6.8	−5.78	−7.9	−4.50
GE	86	73	55	68	91	96	118	61	85	52	−7.5	−6.23	−8.2	−4.75
GH	113	65	61	66	55	38	101	106	104	64	−7.2	−5.97	−8.3	−4.90
GP	77	47	67	105	83	93	92	67	19	88	−7.5	−6.13	−7.2	−4.14
GW	134	71	70	30	70	75	117	54	42	115	−7.5	−5.77	−8.1	−4.37
GR	61	81	64	64	65	28	47	37	112	99	−6.7	−5.47	−6.5	−3.62
GJ	68	54	64	62	91	77	83	42	107	92	−6.8	−5.63	−8.0	−4.59
GV	86	71	73	61	62	68	90	78	93	83	−7.1	−5.92	−8.2	−4.65
NP	77	54	60	80	60	52	100	122	114	76	−6.6	−5.01	−9.3	−4.77
NE	56	69	59	87	86	55	88	60	36	85	−7.1	−4.93	−6.5	−3.21

obtain the best fit to the data for all counties. One might worry about utilizing 56 adjustable constants, but with 1,601 pieces of data, the fitting procedure gives values with small statistical uncertainties, including $B = -3.1 \pm 0.6$ for males and $B = -3.5 \pm 0.9$ for females. These reduce the discrepancy with theory by 29% and 31%, respectively. One might therefore conclude that this is an effect of some importance.

However, the statistics literature contains frequent warnings about use of many variables in a multiple regression to quantify the causal relationship of one particular variable. An obvious problem here is that, since there is a strong negative correlation between M and r as indicated by Fig. 1, any SEV that has a strong correlation with M is likely to have a strong correlation of opposite sign with r. In fitting eqn (7), its term will therefore "drain away" some of the strength of the Br term, reducing the value of B. With many such variables acting in that way, the value of B may be substantially reduced.

This problem was investigated in some depth utilizing the data for males, beginning with a determination of the coefficients of correlation (R) of each SEV with M (CORR-M) and with r (CORR-r). These are plotted in Fig. 2, where a clear pattern is evident—there is a very strong tendency for an SEV with a large CORR-M to have a large CORR-r of opposite sign.

To study the problem further, the number of SEV is first truncated to reduce computational labor by keeping only the 13 SEV in Fig. 2 that have $|\text{CORR-}M| > 0.125$ (points encircled). It is these SEV which we expect to be most important in the problem outlined above. In fact, if only these 13 SEV are retained in eqn (7), B is changed from -7.3 (simple regression) to -3.7 ± 0.6, which is 86% of the reduction from keeping all 54 SEV.

A model is then introduced based on artificial SEV which have a built-in CORR-M but no built-in CORR-r. The SEV are first "standardized"—let X = [X-mean(X)]/[SD(X)]—and several hundred artificial SEV, SEV(art), are generated for each county as

$$\text{SEV(art)} = p\,M + (1 - |p|)\ \text{sample-}M, \qquad (8)$$

where sample-M is a random sample of the M-values from the 1,601 counties (each used only once) and p is given several different values between -0.25 and $+0.25$. Five sets of 13 SEV(art) are then selected from this list such that in each set, there is one SEV(art) which has the same CORR-M as one of the actual 13 SEV. Note that these SEV(art) have no built-in CORR-r; any CORR-r they may have must derive only from the correlation between M and r.

When these sets of SEV(art) are used in eqn (2), the values of B obtained are -5.2 ± 0.5, -5.1 ± 0.5, -4.9 ± 0.5, -5.0 ± 0.5, and -4.9 ± 0.5. Thus, utilizing these SEV(art) which have no built-in CORR-r, reduces B from -7.3 to -5.0, which is 64% of the reduction obtained from using our actual SEV. An alternative procedure based on 17 SEV by adding points surrounded by squares in Fig. 2, selected because of their large CORR-r, gave a reduction of B from use of these SEV(art) that is 73% of the reduction obtained by use of the actual SEV. It therefore seems reasonable to conclude that about two-thirds of the 29% reduction in our discrepancy obtained from use of multiple regression is due to the methodological problem under investigation. Thus the actual effect of confounding by combinations of SEV is to reduce the discrepancy by perhaps 10%.

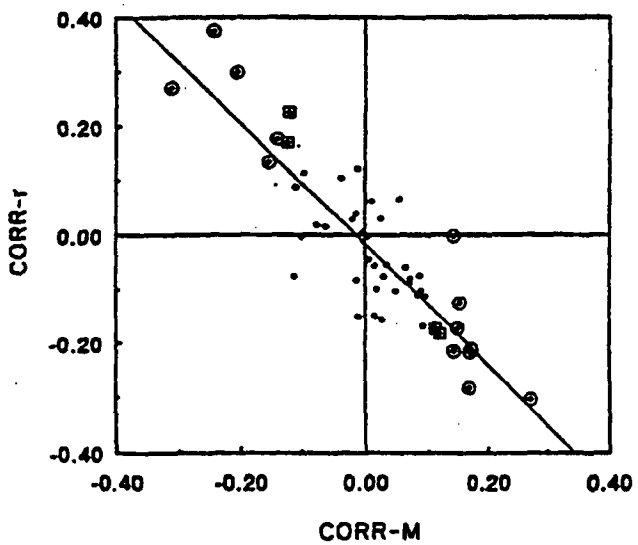

Fig. 2. CORR-r vs. CORR-M for the 54 socioeconomic variables (SEV). Circles and squares around some of the points are to refer to those points in the text.

J. Confounding by geography

The only thing known to correlate strongly with r is geography (Cohen 1991), which suggests that it be considered as a CF. It is therefore treated by the stratification method used above for SEV. The U.S. Bureau of Census divides the nation into four regions, each consisting of two or three divisions. In the previous study (Cohen and Colditz 1994) it was found that stratifying on divisions reduced the discrepancy for males and females by 22% and 16%, and stratifying to the level of individual states reduced it by 28% and 17%, respectively.

Table 4. Results of stratifying on geography by regions and by divisions. The bottom two rows are the averages of results for the four regions and for the nine divisions.

Region Division	Number of counties	Male		Female	
		B	t	B	t
Northeast	215	−6.0	−5.72	−9.9	−5.63
New England	65	−3.0	−0.81	−0.5	−0.06
Mid Atlantic	150	−6.1	−5.11	−11.6	−6.01
North Central	612	−5.1	−6.10	−5.4	−4.80
East NC	308	1.2	1.02	1.6	1.06
West NC	304	−6.0	−4.81	−5.8	−3.26
South	566	−7.9	−6.02	−8.7	−4.71
South Atlantic	273	−9.2	−3.90	−5.2	−1.58
East S. Central	135	−1.9	−1.07	−6.8	−2.54
West S. Central	158	−14.4	−6.02	−15.3	−4.47
West	208	−5.5	−3.36	−8.1	−2.86
Mountain	167	−1.3	−.069	−6.7	−1.83
Pacific[a]	41	0.6	.150	−9.3	−1.43
Averages					
Regions		−6.1	−5.30	−8.0	−4.50
Divisions		−4.4	−2.21	−6.6	−2.23

[a] Includes only WA and OR.

In the present analysis, there are data for nearly tw[illegible] as many counties, which greatly improves the st[illegible]ics. The results of stratifying on regions and on div[illegible]ons are listed in Table 4. Averaging over B values for the 4 regions reduces B from −7.3 to −6.1 for males, and from −8.0 to −6.6 for females, reducing the discrepancy by 8.2% and 9.0% respectively. Averaging B-values for the 9 divisions reduces B from −7.3 to −4.4 for males, and from −8.3 to −6.6 for females, reducing the discrepancy by 19.9% and 10.9% respectively, somewhat less than in the previous study.

In the present data base, there are 34 states with at least 20 counties having known radon levels, as compared with only 18 states in the previous study. The results for individual states are listed in Table 5. Averaging over B-values for these 34 states gives B = −6.1 for males and −7.2 for females, which now reduces the discrepancy by only 8.2% and 7.1% respectively, far less than in the previous study.

Table 5. Results of stratifying on geography to the level of individual states. All states with at least 20 counties in the data file are included.

		Male		Female	
State	Number	B	t	B	t
AL	38	−5.3	−1.05	−1.5	−0.16
AR	36	−14.6	−2.96	−13.8	−1.85
CA	44	−2.9	−0.47	−19.6	−1.71
CO	41	−1.4	−0.42	−8.9	−1.84
FL	33	−1.2	−0.23	3.5	0.65
GA	52	−12.4	−2.46	−5.9	−0.65
ID	40	2.1	0.45	−8.2	−1.04
IL	54	−3.1	−1.07	−5.2	−1.31
IN	58	0.0	0.01	1.7	0.54
IA	98	−3.8	−1.99	−5.0	−1.52
KS	21	−12.1	−1.85	−16.1	−2.20
KY	32	−3.2	−1.07	−10.7	−2.63
LA	21	−20.8	−0.73	−42.6	−0.90
MD	24	−11.5	−1.83	−12.2	−2.14
MI	53	3.2	1.02	0.3	0.09
MN	64	−2.1	−1.40	−10.1	−3.84
MO	31	−9.6	−1.19	−6.8	−0.57
NB	43	−2.3	−0.50	−2.7	−0.48
NJ	21	−0.3	−0.09	−2.6	−0.49
NM	30	−2.9	−0.60	−2.1	−0.19
NY	62	0.7	0.25	−8.2	−1.46
NC	54	−9.1	−2.54	2.8	0.64
ND	39	−5.3	−1.41	22.6[a]	2.60
OH	88	0.0	−0.02	−0.2	−0.10
OK	43	−12.6	−1.87	−24.1	−2.60
PA	67	−1.5	−1.07	−5.3	−2.32
SC	36	−37.9	−2.43	−0.7	−0.03
TN	46	0.4	0.16	−4.8	−1.18
TX	58	−10.4	−3.14	−11.7	−2.56
VA	66	−6.1	−1.43	−15.0	−1.93
WA	29	−5.4	−1.55	−12.8	−1.85
WV	37	0.2	0.05	−10.4	−1.91
WI	55	−9.6	−2.05	−4.9	−0.70
WY	21	−5.9	−1.02	−4.9	−0.37
Averages		−6.1	−1.08	−7.2	−1.07

[a] This is dominated by a single rural county in which there was one death over the 10-y period. If that county is deleted, B = 5.5, t = .074.

Perhaps the most important point is that in the previous study it seemed like the finer the stratification on geography, the less the discrepancy became. But now with a much larger data base giving much better statistics, that trend is reversed, with the finest stratification reducing the discrepancy by only about 8%.

Since our S-values for counties are calculated as the S-value for the state plus a correction for "%-urban", it has been suggested that our analyses for individual states does not adequately adjust for smoking variations among the counties of the state. Since the correction is derived from lung cancer rates, there is good reason to believe that it is reliable. However, as a test of sensitivity to this problem, the correction was doubled as in the related test discussed in section G. The effects on Table 5 were relatively minor; the average of the B-values (bottom line of Table 5) was changed from −6.1 to −5.7 for males, and from −7.2 to −6.4 for females.

K. Confounding by physical features

Apart from smoking, socioeconomics, and geography, another type of potential confounding factor is physical features of the location like barometric pressure (which is determined by altitude), temperature, precipitation, etc. Unfortunately, no data on these were found for counties, but there are data for the most important cities in each state (U.S. Census 1982), which are averaged to obtain values for states. To use these, the project must be reconsidered as dealing with states rather than with counties.

To be consistent with the study of counties, data for Arizona, California, and Florida are deleted, and because of a misunderstanding, Alaska and Hawaii were also deleted, but in retrospect this may be justified by the fact that, in many ways, they are not typical of the other states. That leaves 46 states (including DC), a very small number of data points in comparison with the 1,601 in the study of counties, which means that statistics are a potential problem.

Applying the treatment used for counties to this data set gives $B = -13.0 \pm 2.3$ for males and -14.4 ± 2.7 for females. These are much larger negative values than were obtained from the data on counties, making the discrepancy larger, but they agree well with the B-values for states in Cohen and Colditz (1994), −12.0 and −14.4, derived from a much smaller data base on radon levels.

The physical features considered here are altitude above sea level, average winter temperature, average summer temperature, centimeters of precipitation per year, number of days per year with more than 0.25 mm precipitation, average wind speed, and percent of time with sunshine as compared with the maximum possible. The data are stratified into three equal groups of 15–16 states, those with the lowest, highest, and mid-range values of the feature under consideration, and the data in each group are fit to eqn (6) to determine B.

Table 6. Results from stratifying data for states on the basis of physical features, listed in column (1). See explanation in text.

				Males			Females		
Stratify on . . .	Ranks	Min	Max	B	SD	R^2 (%)	B	SD	R^2 (%)
Altitude (m)	1–15	5.5	65	−6.1	4.8	4	−21.9	9.5	30
	16–31	65	140	−7.1	3.9	19	−8.5	5.3	16
	32–46	158	632	−13.7	3.4	55	−16.3	4.5	50
	1–31	5.5	140	−8.9	3.4	18	−13.0	4.2	25
	39–46	320	632	−16.0	7.6	42	−8.1	6.5	9
Temp.-Jan. (°C)	1–15	−13.2	−3.0	−11.1	3.7	41	−13.9	4.1	47
	16–31	−2.3	0.8	−18.4	4.2	58	−19.5	4.1	61
	32–46	1.4	11.6	−14.5	5.4	35	−1.9	6.3	1
	1–7	−13.2	−6.7	−9.8	4.9	44	−7.3	3.2	51
	40–46	5.2	11.6	−45	16	61	−64	17	74
Temp.-July (°C)	1–15	19.5	22.7	−17.3	4.4	54	−18.2	5.5	46
	16–31	22.8	25.1	−14.9	3.0	63	−18.9	2.8	77
	32–46	25.6	46.2	−14.4	5.3	36	−3.7	1.8	2
Precipitation (cm y^{-1})	1–15	18.3	77.7	−11.7	3.7	44	−15.3	5.3	39
	16–32	78.2	103.6	−5.1	3.6	11	−10.7	4.5	28
	33–46	108.0	170.2	−12.2	6.8	20	−20.4	8.5	33
	1–8	18.3	41.1	−10.5	6.2	33	−11.9	11.9	15
Precipitation (d y^{-1} >0.25 mm)	1–16	51	105	−10.5	3.4	41	−12.8	4.3	39
	17–31	110	124	−9.0	6.9	12	−22.0	7.9	37
	32–46	124	154	−14.7	6.4	29	−11.7	7.8	15
	1–8	51	90	−13.6	2.3	85	−7.4	8.1	12
	9–16	95	105	−12.4	5.6	44	−14.5	5.4	56
Wind (m/s average)	1–15	2.9	3.9	−13.6	7.2	21	−13.7	8.6	17
	16–30	4.0	4.4	−12.5	3.9	43	−9.8	5.4	20
	31–46	4.5	5.8	−13.6	3.6	50	−17.1	3.6	63
Sunshine (%)	1–15	49	57	−14.7	5.1	40	−16.4	7.1	29
	16–31	57	62	−12.1	3.4	48	−17.5	3.4	66
	32–46	62	81	−12.7	4.2	41	−5.2	5.7	6

Results are shown in Table 6. For example, the first section involves stratifying on altitude and the top row gives results for the 15 states with the lowest altitude (ranks 1–15), in which the minimum and maximum altitudes are 5.5 m and 65 m above sea level; the data for males in this group is fit by $B = -6.1 \pm 4.8$ (one standard error, SE), and R^2, the percent of the variation in the data explainable by the simple linear relationship, is 4%; the data for females is fit by $B = -21.9 \pm 9.5$, with $R^2 = 30\%$. In addition to the stratification into three equal groups with lowest, mid-range, and highest values of the feature under consideration which appear in the top three rows of each section, results for other groupings are also shown in some of the sections where these are judged to be useful. For example, in the fourth section of Table 6 on precipitation, the values for the 15 states with lowest precipitation ranged from 18.3 to 77.7 cm y^{-1}, a very wide variation; a grouping of the 8 states with the lowest precipitation, ranging from 18.3 to 41.1 cm y^{-1} is therefore added.

A total of 28 groupings is included in Table 6. For both sexes, this gives 56 values of B and all 56 are negative. The average value of B for the three equal size groups for males [females] is −9.0 [−15.6] for altitude, −14.7 [−11.8] for winter temperature, −15.5 [−13.6] for summer temperature, −9.7 [−15.5] for mm y^{-1} of precipitation, −11.4 [−15.5] for d y^{-1} of precipitation, −13.2 [−13.2] for wind speed, and −13.2 [−13.0] for %-sunshine. In no case do these deviate from the values without stratification, −13.0 [−14.4], in the same direction for both males and females, and in no case is the average deviation for the two sexes more than 0.6 standard deviations.

These studies therefore lead to the conclusion that none of the physical features is an important confounding factor in the relationship between lung cancer and radon exposure. The strong decrease in lung cancer rates corrected for smoking frequency with increasing radon exposure is found if we consider only the low altitude states or if we consider only the high altitude states; if we consider only the warmest or if we consider only the coldest; if we consider only the wettest or only the driest; etc. It is also found if we consider only states where these features are close to average.

L. Effects of recognized *r-S* correlations

Extensive studies have been previously reported on how house characteristics, locations, socioeconomic factors, etc., correlate with radon levels in homes (Cohen 1991). There were two of these factors that one would expect to correlate with lung cancer incidence: (1) urban houses have 25% lower radon levels than rural houses, and urban people smoke more frequently; and (2) houses of smokers have 10% lower radon levels than houses of non-smokers, which is a direct radon-smoking correlation on the level of individuals (as opposed to a correlation on the level of

counties). Other potential confounders could be considered here, such as income or education: poor and less educated people smoke more than average. However, little difference was found in mean radon levels as a function of income, value of house, or education, and the relationships are not monotonic—e.g., middle income people have the highest radon levels. Furthermore, these factors should be taken into account by the numerous SEV.

To calculate the effects of factors (1) and (2), a model is introduced in which it is assumed that the BEIR IV formula gives the correct lung cancer risk, and that variations in smoking prevalence are determined only by urban vs. rural considerations. While this model is highly oversimplified, it includes all the elements relevant to the effects we are studying. It only makes use of the data on average radon levels, r, and the percentage of population living in urban areas, PU, for each county.

It is assumed that the mean radon levels are xr_m for rural areas and r_m/x for urban areas of a county, where r_m is the measured value for the county as a whole. For males, it is assumed that the smoking frequency, S, is 0.5 y in urban areas (where 0.5 was the national average smoking frequency) and 0.5 y^{-1} in rural areas. (For females 0.5 is replaced by 0.32.) Both x and y are normally greater than unity, and they are treated as parameters. For x, the best estimate is 1.12. Regression analysis on data for counties indicates that as PU goes from 0–100%, male lung cancer rates go from 53–66 y^{-1} per 100,000, a variation of ± 10% from the average; this is interpreted to indicate proportional prevalences of smoking, or $y = 1.10$.

In order to treat factor (2), it is assumed that the above values of r are multiplied by z for smokers and divided by z for non-smokers. The best estimate is $z = 1.05$.

The derivation of eqn (3) treated two groups, smokers and non-smokers, but here this is increased to four groups, urban smokers (US), urban non-smokers (UN), rural smokers (RS), and rural non-smokers (RN). The percentage, P, in each category is

$$P(\mathrm{US}) = \mathrm{PU}(0.5\,y)$$
$$P(\mathrm{UN}) = \mathrm{PU}(1\text{–}0.5\,y)$$
$$P(\mathrm{RS}) = (1\text{-PU})\,(0.5\,y^{-1})$$
$$P(\mathrm{RN}) = (1\text{-PU})\,(1\text{–}0.5\,y^{-1}).$$

The average radon level for each category is

$$r(\mathrm{US}) = r_m/xz$$
$$r(\mathrm{UN}) = r_m z/x$$
$$r(\mathrm{RS}) = r_m x/z$$
$$r(\mathrm{RN}) = r_m xz.$$

The average radon level for the county, to be used in the regression, is then $r = P(\mathrm{US})r(\mathrm{US}) + P(\mathrm{UN})r(\mathrm{UN}) + P(\mathrm{RS})r(\mathrm{RS}) + P(\mathrm{RN})r(\mathrm{RN})$, and the smoking prevalence, S, is $S = P(\mathrm{US}) + P(\mathrm{RS})$. We can then calculate m_0 from eqn (5).

The mortality rate for each category is

$$m''(\mathrm{US}) = a_s\,[1 + .073r(\mathrm{US})]$$
$$m''(\mathrm{RS}) = a_s\,[1 + .073r(\mathrm{RS})]$$
$$m''(\mathrm{UN}) = a_n\,[1 + .073r(\mathrm{UN})]$$
$$m''(\mathrm{RN}) = a_n\,[1 + .073r(\mathrm{RN})],$$

and the county mortality rate to be used in the multiple regression is $m = P(\mathrm{US})m''(\mathrm{US}) + P(\mathrm{UN})m''(\mathrm{UN}) + P(\mathrm{RS})m''(\mathrm{RS}) + P(\mathrm{RN})m''(\mathrm{RN})$.

Note that the radon level r is not quite the same as the measured value, r_m, but for x, y, z not very different from unity, it is close. The only important thing for our model is that the distribution of r-values for all counties is realistic.

Once m, r, and m_0 have been calculated for each county, the slope, B, of the regression of m/m_0 on r and the slope, B', of the regression of m on r can be determined. The values of B and B' for males and females are listed in Table 7. In that Table, section A, $x = y = z = 1$, is the baseline situation, section B gives the urban-rural effect, section C gives the effect of the radon-smoking correlation, and section D combines both of these effects. The top entry in each section is based on the best estimates (BE), and succeeding lines treat deviations from unity of 2 × BE, 4 × BE, 8 × BE, and 16 × BE.

We see that the urban-rural effect reduces B' by about 18% with the BE, and for more than 4 × BE it reduces the slope to zero, but the correction for smoking, using m/m_0, compensates for these effects causing B to be almost unaffected.

Factor (2), the radon-smoking correlation on the level of individuals, has a much lesser effect on B', reducing it only to 60% of its baseline positive value even if the effect is 16 × BE. But it has a stronger effect on B since it is not related to smoking prevalence and hence is not compensated by our smoking correction. The combination of the two effects studied here gives roughly what might be expected from a linearly independent relationship.

Table 7. Results for model that tests effects caused by known r-S correlations. See discussion in text.

Section	x	y	z	B (male)	B (female)	B' (male)	B' (female)
A	1	1	1	7.0	7.0	4.1	.98
B	1.12	1.1	1	7.0	7.0	3.3	.81
	1.24	1.2	1	6.9	6.9	2.2	.59
	1.48	1.4	1	6.8	6.7	0.23	.02
	1.96	1.8	1	6.5	6.4	−2.5	−.41
C	1	1	1.05	6.7	6.7	3.9	.94
	1	1	1.1	6.5	6.4	3.8	.89
	1	1	1.2	6.0	5.8	3.5	.82
	1	1	1.4	5.1	5.0	3.0	.70
	1	1	1.8	3.9	3.9	2.3	.54
D	1.12	1.1	1.05	6.7	6.7	3.1	.77
	1.24	1.2	1.1	6.3	6.3	1.9	.51
	1.48	1.4	1.2	5.6	5.6	−0.3	.07
	1.96	1.8	1.4	4.5	4.7	−2.8	−.40
	2.92	2.6	1.8	3.4	3.9	−3.6	−.56

It is important to recognize here that the BEs are based on a great deal of data and hence are reasonably accurate, and anything greater than 2 × BE is highly unlikely. This means that B is probably reduced by only 5% as a result of these effects, and a reduction by more than 10% is highly unlikely. The BEIR IV prediction is thus reduced only from +7.3 to about +6.9, which contributes very little to explaining the large negative values of B obtained from the actual data.

Perhaps the most important aspect of this section is that the effects calculated here are typical of the largest effects that can be reasonably expected from confounding factors. Their very small impact on the discrepancy leads to an impression that no confounding relationship can be reasonably expected to resolve that discrepancy.

M. Linear-no threshold theories other than BEIR IV

Up to this point we have considered only the BEIR IV theory, but other linear-no threshold theories have been proposed based on the miner data and differing principally in their treatment of smoking. How specific are the discrepancies reported here to the details of the BEIR IV theory?

A more general form of eqn (1) is

$$m' = a + br' \qquad (9)$$

where both a and b may have different values for smokers and non-smokers. If we proceed as in deriving eqn (3) from eqn (1), but ignoring the correction for migration which is the same for all theories, this leads to

$$m = Sa_s + (1 - S)a_n + [Sb_s + (1 - S)b_n]r$$

which can be re-written

$$m = Sa_s + (1 - S)a_n + [eS/\bar{S} + (1 - e)]b'r \qquad (10)$$

where $\bar{S}$ is the national average value of S, and e, b′ are new constants replacing b_s, b_n. By setting the expressions for m in eqns (10) and (5) equal to each other, we find that eqn (5) is a special case of eqn (10) with b′ = 4.9, e = 0.85 for males, and b′ = 1.17, e = 0.73 for females. The parameter e is an index of the relative risk from radon to smokers and non-smokers; for e = 0 their risks are equal and for e = 1, only smokers are at risk. The true values of e within the range 0 to 1 are a matter of substantial uncertainty, and this fact is clearly acknowledged in the BEIR IV Report. An important advantage of eqn (10) is that the national average value of m is independent of e, as we can see by setting $S = \bar{S}$.

The first two terms in eqn (10) represent risks of smoking unassociated with radon exposure, a matter that has been thoroughly studied and is subject to little uncertainty. The factor b′ in eqn (10) is derived directly from the miner data, with little sensitivity to the value of e, and it is therefore not uncertain by more than about 50%. Thus, by varying e between 0 and 1, and varying b′ over a relatively small range, we should include any linear-no threshold theory based on the miner data. We proceed by using the data on males and determining the ratio of observed m to values of m calculated from eqn (10), o/c, for each state. We then determine the slope, B'', of the best straight line fit to o/c vs. r. If theory is correct, it should be zero.

When we set b′ equal to the BEIR IV value and decrease e in steps from 1 to 0, B'' varies only from −0.16 to −0.17. There is essentially no sensitivity to the value of e.

We then set e equal to the BEIR IV value, 0.84, and multiply b′ by a factor f. As f is decreased from 2 to 1 to 0.5 to zero, the slope B'' changes only from −0.195 to −0.168 to −0.148 to −0.120. If we restrict our consideration to the maximum expected variation of ±50%, the variation is only between −0.184 and −0.148.

We conclude that our discrepancy between observation and theory would apply with only minor differences to any linear-no threshold theory derived from the miner data. The reason for this is easy to understand: the principal difference between various models is that they give widely different treatments of smoking, but since the r-S correlation is relatively small, this has little impact on the relationship in Fig. 1 between radon exposure and lung cancer rates.

A more direct way to avoid dependence of this study on the specific treatment of smoking in BEIR IV is to stratify the data on S and investigate each stratum as an independent data set. Since S-values are then approximately the same for all counties in the same data set, the potential for confounding by S is greatly reduced. The data are stratified into deciles, 10 sets of 160 counties each. For males, B-values in order of increasing S are −5.9, −6.7, −11.0, −5.8, −7.4, −7.6, −6.8, −6.5, −4.0, −6.0, all negative with an average of −6.8, vs. −7.3 without stratification. For females, B-values are −10.5, −4.5, −11.9, −6.7, −10.0, −4.2, −7.5, −10.6, −10.4, −6.2, again all negative and with an average of −8.2 vs. −8.3 without stratification.

Clearly, the functional form of S-dependence in the m-r-S relationship derived from the BEIR IV theory is not the cause of the discrepancy. This treatment also avoids effects of the width of the distribution of S-values. However, it does not address the problem of "intensity of smoking." A partial answer to that problem is to stratify on the S-values derived from lung cancer mortality rates described in section G. For males, this process gives an average B = −5.2 vs. −6.0 without stratification, and for females B = −5.3 vs. −6.3. These represent about an 8% reduction in the discrepancy.

N. Requirements on an unrecognized confounder

It is, of course, logically possible that there is some unrecognized confounding factor that can explain the discrepancy. This is a logical possibility in

any type of epidemiological study, and few of these have included as thorough an investigation of confounders as has been done here.

However, it is interesting to consider the properties required of a confounder to resolve the discrepancy:

1. It must have a very strong correlation with lung cancer, comparable to that of cigarette smoking, but still be unrecognized.
2. It must have a very strong correlation of opposite sign with radon levels.
3. It must not be strongly correlated with any of the 54 socioeconomic variables (SEV).
4. It must be applicable in a wide variety of geographic areas and independent of altitude and climate.

How credible is the existence of such an unrecognized confounder? Requirement number 1 alone severely strains its credibility, since tremendous effort has gone into lung cancer studies. This unrecognized confounder must have increased by orders of magnitude since the beginning of this century, have been much more important in males in the first half of the century, with effects on females rapidly catching up in recent years; these are all very difficult requirements, fulfilled, to our knowledge, only by smoking. There has also been extensive study of factors that may correlate with radon levels, and other than geography, all correlations have been rather weak. There is no readily apparent reason, aside from the factors considered in section L, why any of them should correlate strongly with lung cancer rates.

Since all SEV correlate strongly with some other SEV, requirement number 3 essentially eliminates all socioeconomic variables and factors that correlate with them such as air pollution. The great majority of confounding factors that have been found to be important in epidemiology are of this type. Thus requirement number 3 is an important restriction. Requirement number 4 gives further important restrictions.

It therefore seems reasonable to conclude that the existence of an unrecognized confounding factor that would resolve the discrepancy is all but incredible. At least it is far less credible than failure of the linear-no threshold theory in the low dose-low dose rate region for radon decay products where that theory has never been verified.

P. Problems with ecological studies

In addition to the problems discussed in section A, several other potential problems with ecological studies have been pointed out by Morgenstern, Greenland, and Robins (Morgenstern 1982; Greenland and Morgenstern 1989, 1991; Greenland 1992; Greenland and Robins 1994). These authors give them names like effect modification, non-linearity and non-additivity, misclassification, divergent bias, cross-level bias, specification bias, standardization, etc. Some of these issues have been reviewed recently by Stidley and Samet (1993).

The basis for these papers is that an ecological study is not mathematically equivalent to an individual-level study, and they point out problems this can cause. For perspective, it is important to recognize that an individual-level study is certainly not mathematically equivalent to the logically correct approach, deriving a risk estimate from a complete knowledge of all causative factors and of how they interact; the problems this can cause are far more important and far less susceptible to treatment. All epidemiology studies only give what lawyers call "circumstantial evidence"—even if all evidence is absolutely correct and accurate, conclusions drawn from it are not mathematically certain. However, epidemiology is a very successful science and has saved many millions of lives. Judgements of epidemiology studies can, and must, be made on the basis of plausibility, and a highly plausible case can be built up from circumstantial evidence.

Of course, it is very important that careful consideration be given to the issues raised by the above authors. They have been examined and found not to be very important in this work. Some of these findings have been published elsewhere (Cohen 1990b, 1992b, 1994a), but they are reviewed here and in Appendix C.

The most important of these effects, called "non-linearity," is the equivalent of the problems discussed in section A applied to confounding factors (CF)—the average value of a CF for a county does not necessarily determine its confounding effects. For example, the effects of family income as a CF may depend on those with very low income rather than on the county average income which may be influenced by a few people with high income. This problem is handled here by including as potential CF, percent below poverty level, percent unemployment, and median income, as well as average income. Other examples of this type are readily apparent from Appendix B for age, for education, etc.

Other types of examples of the problems discussed in section A applied to confounding factors are the cases treated in section M where their effects are found to be very small. Note that this problem does not apply to the principal variables in this work, r and S, because linearity with r is the theory being tested, and S arises from exact mathematics in converting risk to individuals into county mortality rates. It might also be noted that very few of the case-control studies of the radon-lung cancer relationship even consider confounding by socioeconomic variables, let alone the very wide variety of them treated here.

Other issues raised by Morgenstern, Greenland, and Robins are discussed in Appendix C. Efforts were made to develop other scenarios that might explain the discrepancy, but without success. Appeals were made to the authors of the papers cited above begging for suggestions, but none were received.

Negative slopes for m vs. r, like those observed here have also been reported from similar but much smaller studies in England (Haynes 1988) and France (Laterjet 1992; Dousset 1990).

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APPENDIX A
Sum Over the Right Side of Eqn. (1)

We evaluate the right side of Eqn. (1), R, which is

$$R = \sum_i g(A_i)[1 + h(A_i)r_i] \qquad \text{(A-1)}$$

We divide the population into age groups, A_j, each of which includes N_j individuals all having essentially the same values of g and h in (A-1); we call these values g_j and h_j. This reduces (A-1) to

$$R = \sum_j N_j g_j + \sum_j (g_j h_j \sum_{i=1}^{N_j} r_i) \qquad \text{(A-2)}$$

The average radon exposure for the group, r, is defined as

$$r = \frac{1}{N_j} \sum_{i=1}^{N_j} r_i$$

We assume that r is independent of age, which makes it the same for all j. (The derivation could be carried out without this simplifying assumption, but it would be substantially more complex.) Thus

$$R = \sum_j N_j g_j + \sum_j r N_j g_j h_j$$

$$= (\sum_j N_j g_j)[1 + br] \qquad \text{(A-3)}$$

where

$$b = (\sum_j N_j g_j h_j) / \sum_j N_j g_j \qquad \text{(A-4)}$$

Note that

$$\sum_j N_j g_j = \sum_{i=1}^{q} g_i$$

which is just the total number of deaths, which is proportional to q.

We absorb the proportionality constant into a_n in Eqn (1) which is still to be evaluated. Thus, (A-3) becomes

$$R = q(1 + br) \qquad \text{(A-5)}$$

In Table A-1, g_j and h_j are taken from Table 2-4 of BEIR-IV utilizing the widely used conversion factor, 1 pCi L^{-1} = 0.2WLM y^{-1} (WLM = working-level-months), which is based on 75% occupancy, and radon daughters at 50% of the equilibrium concentration with radon gas. Col. (1) lists the age ranges for the various groups, j, with A_j taken to be in the center of the range. Col. (2) is h_j from BEIR-IV expressed as the percent increase of risk per unit of radon exposure, $\%/r_0$, (%/pCi L^{-1}). Col. (3) is the life table population of each age group, which is proportional to N_j. Col. (4) is the lung cancer rate for that age range which is proportional to g_j. Note that absolute values are not required here for N_j and g_j as any constant by which they might be multiplied appears in both the numerator and denominator of (A-4) and hence cancels out. Col. (5) is $N_j g_j$, Col. (3) × Col. (4); the sum of this column is 8253. Col. (6) is then $N_j g_j h_j$, Col. (5) × Col. (2) divided by 8253. In accordance with (A-4), the sum of Col. (5) gives b in units of $\%/r_0$.

In calculating a mortality rate for a county, one should use the age distribution for the population in column (3), and the result might be expected to depend on this age distribution, especially the fraction that is elderly. Using the age distribution in the U.S. population (1990) gives b = 10.82. One might think there would be important differences for differ-

Table A-1. Calculation of *b* from Eqn. (A-4).

(1) Age range (y)	(2) % increase per r_0	(3) Population (life table)	(4) Lung CA rate 10^{-5} y^{-1}	(5) (3) × (4)	(6) (2) × (5) / 8,253
0–15	3	1480	.0002	0	.000
15–25	7.5	980	.0009	1	.001
25–35	10.5	969	.008	8	.011
35–45	13.5	953	.125	119	.189
45–55	16.5	919	.75	689	1.37
55–65	16.3	840	2.17	1,823	3.60
65–75	7.5	687	4.10	2,817	2.56
75–85	8.5	440	4.85	2,134	2.20
85–95	9.5	150	3.68	552	.64
95–105	10.5	(30)	(3.68)	110	.14
			Sum:	8,253	10.72

ent states. The states with the highest and lowest percentage of population over age 65 (excluding Florida and Alaska, which we exclude from our data file) are Pennsylvania (14.8%) and Utah (8.2%). Utilizing the current age distribution for those states in column (3) of Table A-1 gives 10.78 for PA and 10.90 for UT. The largest difference in age distributions we might encounter is between males and females. Utilizing current national data for these gives b = 11.10 for males, b = 10.64 for females.

All of the above values of b are essentially identical well within other uncertainties in our treatment. Adopting a single value avoids a great deal of computing and makes our analysis much more transparent. We therefore adopt a single value, b = 10.8.

It is useful to recognize that Table A-1 can also be used to calculate the lifetime risk to an individual, m*. From Eqn (1), dropping the subscript i,

$$m^* = a_n \sum_{A=1} p(A)g(A)[1 + h(A)r'] \qquad \text{(A-6)}$$

where p (A) is the probability that the individual will be alive at age A. To evaluate this sum, we divide ages into age ranges, j, and let N'_j = number of years an individual expects to be alive in age range j, which is just p (A) times the number of years in the range.

Then (A-6) becomes

$$m^* = a_n[\sum_j N'_j g_j + r' \sum_j N'_j g_j h_j]$$

$$= a_n(\sum_j N'_j g_j)[1 + b'r']$$

where

$$b' = \frac{\Sigma_j N'_j g_j h_j}{\Sigma_j N'_j g_j} \qquad \text{(A-7)}$$

Eqn (A-7) can be evaluated with Table A-1 as was done above for Eqn (A-4), recognizing that Col. (3) is proportional to N'_j, and that the proportionality constant cancels out in Eqn (A-7). Thus, Eqn (A-4) gives the same result as Eqn (A-7), and b' = b = 10.8.

This fact is useful because lifetime risks are tabulated in BEIR-IV, Table 2-4 (revised), and values of b' are readily obtained there. One can see that b = b' = 10.8 for males and females, smokers and non-smokers.

APPENDIX B
Socioeconomic Variables (SEV) Used in This Work

Population characteristics
PT = Total population
PD = Population km^{-2}
PI = % Pop. increase 1980–1986
PU = % in urban areas
PW = % white
PS = males per 100 females
PE = % age >64 y
PO = % age >74 y
PY = % 5–17 years old
PN = % born in state
PH = Persons per household

Vital and health statistics
VB = Births per 1,000 people
VC = % births to mothers <20 y
VD = Deaths per 1,000 people
VI = Infant deaths per 1,000 births
VM = Marriages per 1,000 people
VS = Divorces per 1,000 people
VP = Physicians per 100,000 people
VH = Hospital beds per 100,000 people

Social
SS = Social Sec. benefit per 1,000 people
SC = crimes per 100,000 people
SH = % high school grad.
SU = % college grad.
SE = $/cap. for education

Housing
HO = % owner occupied
HA = % with >1 automobile
HV = median value ($)
HN = % <8 y old

Economics
EI = $ per capita income
EH = Median household income ($)
EJ = % persons below poverty level
EV = % families below poverty level
EU = % unemployment
EW = average salary, wage
EP = $ per capita personal income
EM = % earnings from manufacturing
ER = % earnings from retail trade
ES = % earnings from services
EG = % earnings from government
EF = % earnings from farming
EA = average acres per farm
EL = % of manufacturing firms >100 employees
ED = $/cap. sales—food stores
EC = $/cap. sales—clothing
EX = $/cap. sales—eating, drink

Government
GF = Federal govt., $/cap.
GL = Local govt., $/cap.
GE = % local govt. expenditure—educ.
GH = % local govt. expenditure—health
GP = % local govt. expenditure—police
GW = % local govt. expenditure—welf
GR = % local govt. expenditure—roads
GJ = local govt. employment per 10,000 people
GV = % vote for lead party, 1984

NP = num. of measurements—PITT
NE = num. of measurements—EPA

APPENDIX C
Response to Issues Raised by Greenland, Morgenstern, and Robins

Greenland and Robins (1993) point out several potential problems with ecological studies. We respond to them here, referring to their examples by the numbers they use:

Non-linearity and non-additivity—examples 1–5

The non-linearity problem for confounding factors has been discussed in Sec. P, and the response to the less important non-additivity problem would be similar. There is no use of additivity here except, very obliquely, in Sec. I.

One problem here with Greenland and Robins (1993) is that, in their examples 3–5, they use a dependence of lung cancer risk on cigarettes per day smoked which is grossly different than the known dependence (Kahn 1966). They are only trying to demonstrate a mathematical inconsistency, but mathematical inconsistency is not an important issue here. The most any epidemiology study can achieve is a high degree of plausibility, and this requires use of plausible input. If one is free to concoct examples without this restriction, any epidemiological study can be shown to give arbitrarily large errors.

Measurement error—example 6

This would be a problem in our work if r were a dichotomous variable, but it is not. The effect of measurement error on r is discussed in Sec. E.

Our smoking variable, S, is a dichotomous variable, but the effects of uncertainties in it are given elaborate consideration in Sec. H.

Cross level bias—examples 7–8

These are not applicable to our work because the public knew nothing about radon in the relevant time period (prior to 1980) and therefore radon levels could not have influenced their actions.

"Misconceptions"

The non-linearity issue was discussed above in connection with examples 1–5. We have made essentially no use of the test of fit, R^2. We do not assume that using a large number of regions eliminates correlations with r—correlations with r are discussed in several sections of this paper, but especially in Sec. H, J, and M. The paper they reference (Cohen 1992b) merely pointed out that the extremely strong r-S correlations they concocted could occur by chance in the three county system they considered, but is much less likely to occur by chance in a much larger system. There is no assumption in any of our work that region is a confounder on the individual level.

Other papers by Greenland and Morgenstern referenced in Sec. P raise other issues or use different names. We discuss their application to this paper here:

Specification bias

This deals with a situation where m is not linearly dependent on r. Since we are testing the linear theory, that problem is not applicable here.

Effect modification

This deals with product terms in the expression for risk to an individual; for example, his risk, m′, might depend on (r′ × s′) where r′ and s′ are his exposure to radon and cigarettes respectively, or on (r′ × A′) where A′ is his age. They point out that such terms cannot be represented in an expression for average risk, m, by products of average values—(r × S) or (r × A) in these examples.

But there is no attempt to do that in this paper. The treatment of smoking is derived from the risk to an individual by rigorous mathematics. In averaging risks over the total population of a county, the age dependence of the risk to individuals can only lead to a dependence on the age distribution of the population, and this dependence is well handled by stratifying on the variables PE, PO, and PY listed in Appendix B.

Misclassification

This is basically another name for "measurement error" discussed above.

Standardization

The application in this paper could derive from the fact that lung cancer rates are age-standardized, while the other variables used are not. It is very difficult to image how that could be an important problem here, but in any case, the problem is removed by stratifying on our age-distribution variables, PE, PO, and PY.

Heterogeneity of exposure within regions

This cannot be a problem with a linear—no threshold theory. The distribution of exposures is completely irrelevant.

■ ■

RADIATION RISK IN PERSPECTIVE

POSITION STATEMENT OF THE HEALTH PHYSICS SOCIETY*

HEALTH PHYSICS SOCIETY

Adopted: January 1996

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Scientific & Public Issues Committee
Health Physics Society

In accordance with current knowledge of radiation health risks, the Health Physics Society recommends against quantitative estimation of health risks below an individual dose of 5 rem[1] in one year or a lifetime dose of 10 rem in addition to background radiation. Risk estimation in this dose range should be strictly qualitative accentuating a range of hypothetical health outcomes with an emphasis on the likely possibility of zero adverse health effects. The current philosophy of radiation protection is based on the assumption that any radiation dose, no matter how small, may result in human health effects, such as cancer and hereditary genetic damage. There is substantial and convincing scientific evidence for health risks at high dose. Below 10 rem (which includes occupational and environmental exposures), risks of health effects are either too small to be observed or are non-existent.

Current radiation protection standards and practices are based on the premise that any radiation dose, no matter how small, can result in detrimental health effects, such as cancer and genetic damage. Further, it is assumed that these effects are produced in direct proportion to the dose received, i.e., doubling the radiation dose results in a doubling of the effect. These two assumptions lead to a dose-response relationship, often referred to as the linear, no-threshold model, for estimating health effects at radiation dose levels of interest. There is, however, substantial scientific evidence that this model is an oversimplification of the dose-response relationship and results in an overestimation of health risks in the low dose range. Biological mechanisms including cellular repair of radiation injury, which are not accounted for by the linear, no-threshold model, reduce the likelihood of cancers and genetic effects.

[1]The rem is the unit of effective dose. In international units, 1 rem=0.01 sievert (Sv)

Radiogenic Health Effects Have Not Been Observed Below 10 Rem

Radiogenic health effects (primarily cancer) are observed in humans only at doses in excess of 10 rem delivered at high dose rates. Below this dose, estimation of adverse health effect is speculative. Risk estimates that are used to predict health effects in exposed individuals or populations are based on epidemiological studies of well-defined populations (e.g., the Japanese survivors of the atomic bombings in 1945 and medical patients) exposed to relatively high doses delivered at high dose rate. Epidemiological studies have not demonstrated adverse health effects in individuals exposed to small doses (less than 10 rem) delivered in a period of many years.

Limit Quantitative Risk Assessment to Doses at or Above 5 Rem per Year or 10 Rem Lifetime

In view of the above, the Society has concluded that estimates of risk should be limited to individuals receiving a dose of 5 rem in one year or a lifetime dose of 10 rem in addition to natural background. Below these doses, risk estimates should not be used; expressions of risk should only be qualitative emphasizing the inability to detect any increased health detriment (i.e., zero health effects is the most likely outcome).

Impact On Radiation Protection

Limiting the use of quantitative risk assessment, as described above, has the following implications for radiation protection:

(a) The possibility that health effects might occur at small doses should not be entirely discounted. Consequently, risk assessment at low doses should focus on establishing a range of health outcomes in the dose range of interest including the possibility of zero health effects.

(b) Collective dose (the sum of individual doses in an exposed population expressed as person-rem) remains a useful index for quantifying dose in large populations and in comparing the magnitude of exposures from different radiation sources. However, for a population in which all individuals receive lifetime doses of less than 10 rem above background, collective dose is a highly speculative and uncertain measure of risk and should not be quantified for the purposes of estimating population health risks.

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* The Health Physics Society is a non-profit scientific organization dedicated exclusively to the protection of people and the environment from radiation. Since its formation in 1956, the Society has grown to more than 6,800 scientists, physicians, engineers, lawyers and other professionals representing academia, industry, government, national laboratories, trade unions and other organizations. The Society's objective is the protection of people and the environment from unnecessary exposure to radiation, and its concern is understanding, evaluating and controlling the risks from radiation exposure relative to the benefits derived from the activities that produce the exposures. Official Position Statements are prepared and adopted in accordance with standard policies and procedures of the Society. The Society may be contacted at: 1313 Dolley Madison Blvd., Suite 402, McLean, VA 22101; Telephone: (703)790-1745; FAX: (703)790-2672; e-mail: hpsburkmgt@aol.com.

Appendix 3

J. JOHNSON

HEALTH PHYSICS FOUNDED 1956

The Newsletter

Volume XXIII, Number 6 June 1995

IN THIS ISSUE

Innovative Research Needed

Marvin Goldman, Ph.D., Professor Emeritus

The traditionally accepted linear, no-threshold hypothesis as a dose-response model for carcinogenesis is increasingly being questioned. This model dates back to the genetic radiation studies on the fruit fly by H. J. Müller in the 1920s. Genetic effects were found to be linearly related to dose over many orders of magnitude.

Later, as somatic effects such as carcinogenesis became evident, the linear hypothesis was extended to carcinogenic effects. It was reasonable to assume that since the "primordial" lesion appears to be in the DNA, that the same proportionality would exist for carcinogenic as well as genetic effects.

Although the "initial sublesions" in the nucleus may be proportional to dose, it is not certain at this point that cancer development follows a linear dose relationship over many orders of magnitude. Most of our solid radiation cancer data is derived over a single order of magnitude (around 0.5 Gy to 5 Gy). At higher doses survival is compromised and few survive the latent period. At lower doses the possible excess incidence is difficult to quantify.

Since our main human data base on low-LET exposures is almost entirely from acute, high-dose rates, i.e. the A-bomb survivors and medical therapy patients, we have little to go on for low-dose rates other than the consistently non-linear relationship for all radiogenic tumors in experimental animals. Since the observation is not in humans, it is all but ignored.

Since direct epidemiological studies cannot be expected to verify effects at doses which are small fractions of background radiation, we may have to wait for the biomolecular explanation of tumorigenesis steps from initiation to promotion to manifestation for our answer.

As long as there seem to be many steps in the model, I am prepared to entertain the hypothesis that the true universal carcinogenesis curve is curvilinear with an initial shallow slope and the equivalent of a saturation plateau at high levels. Each of the molecular and cellular "steps" that contribute to the data which generate such curves may have its own probability distribution and it may not be linear. The sum of these step probabilities also may not be a straight line – it is just as likely to be sigmoid!

Let's stop debating what we believe and hope for, and put the linear, no-threshold hypothesis to sound, solid scientific scrutiny and objective testing. It is time for innovative research! We need to do a complete review of the available data, and as well employ our newer molecular tools in unique research to better understand the radiation carcinogenesis process. ■

HPS *Newsletter*, Volume XXIII, Number 6, June 1995

EDITORIAL

Dose-Response Model Reactions Bring Surprises

Two notable surprises occurred as responses came in to my editorial in the April issue of the *Newsletter*. The biggest surprise is that responders held very closely to the 500-word limit for submissions and that this limit did not seem to hamper authors. Responses seem cogent and complete.

The second surprise is that the viewpoints are all so one-sided. Almost all refute the linear, no-threshold (LNT) paradigm. We had invited responses from both "sides" of this issue, so don't know how to interpret the lack of reaction from the LNT supporters.

It certainly is a controversial topic. Almost as controversial, we found, is how to punctuate the name of our model under discussion. Submissions had at least three different styles. Health physics publications editors decided it should be "linear, no-threshold."

The 22 responses received by the 1 May deadline appear in the next 14 pages of the *Newsletter*. Regular *Newsletter* materials start on page 17. The first several in the special section give some of the history of the linear, no-threshold model. The next few discuss molecular and cellular implications. The remainder are of a more general nature and are arranged, as much as possible, to look nice on a page. Due to the historical nature of some of the articles, traditional units have been retained.

What use will be made of this special issue of the *Newsletter*? First of all, we hope it will be interesting to read.

Secondly, we have already sent the articles to Ken Mossman, Chairman, Scientific and Public Issues (SPI) Committee, Health Physics Society (HPS). Ken was directed by the Board to prepare a HPS position paper on the subject following a recommendation to this effect by Wade Patterson at the midyear meeting of the Board in Charleston.

Ken expects to have a rough draft of this position paper ready for review by the SPI Committee at the July meeting in Boston. The Committee will decide on the deposition of the paper at that time.

Under consideration will be whether to submit it to the NCRP. The NCRP plans to initiate a new Scientific Committee 1-6, Basis for the Linearity Assumption. It is expected that work on this Committee will begin in the middle of the year. Chairing the Committee will be Arthur C. Upton.

The paper may also be submitted to the National Academy of Sciences as input to the next committee assigned to update the evaluation of low-level effects.

In addition to submitting this special issue to the SPI Committee, what other plans do we have? It is expected that this issue will get a lot of other people excited about the topic and that they will want to put their words on paper. We will continue to entertain submissions. Keep the body of your paper to $\leq$500 words, use references where necessary and follow the style set by *Health Physics*. Avoid duplicating what others have already said.

This special issue put a heavy work load on our small-but-dedicated *Newsletter* staff. Sharon typed until her hands were numb around deadline time. She also introduced needed consistency in the references for the articles. Mary assisted in copy editing and formating the special section.

Associate Editor Andy Hull provided ideas and names of persons to be invited for submissions. Associate Editor Steve Garry carefully proofed all of the submissions. Thanks to all.

Gen Roessler ■

— SPECIAL ISSUE — RADIATION DOSE-RESPONSE MODEL

Through Space and Time... to the Linear, No-Threshold Paradigm

Ronald L. Kathren

It is perhaps not without significance to note that for virtually all health physicists and radiation biologists in active practice today, the linear, no-threshold dose response for low dose and low-dose rate radiations has, throughout their entire careers, been the foundation of radiation protection standards applied in our efforts to protect people and the environment from the harmful effects of radiation. It thus may come as a surprise to some, particularly those who have begun their careers in recent years, to learn that the linear, no-threshold model and its offspring, ALARA and the nontruncated application of collective dose, have not always served as the basis for radiation protection standards.

In fact, the linear hypothesis is a relative latecomer. Initially following the discovery of x rays and radioactivity, the general belief was that radiation exposure was not harmful. This euphoria quickly gave way to the increasing reports from both experimental work and field observations in humans to the more sober conclusion that too great an exposure could, indeed, result in some sort of damage. Thus, although by 1905 it was generally recognized that too great an exposure could result in acute frank effects (today we call them deterministic), it was not until 1925 -- three full decades after the discovery of x rays -- that the first protection standard was proposed. The standard was based on the so-called skin erythema dose and implicitly (and indeed its proposer, Arthur Mutscheller, so stated) carried with it the concept of a dose which, if not exceeded, would permit such damage as might occur to be repaired, or, in other words, a *tolerance dose.*

The concept of the tolerance dose held for nearly three decades. It served the Manhattan District workers well, and seemed to provide an adequate margin of safety. Indeed, 40, or even 30, years ago the prevalent belief was that one could be exposed at the maximum permissible dose (then 15 rem whole body per year) continuously over a 50-year working lifetime with no demonstrable ill effect. But in the 1950s, the linear, no-threshold model was adopted, based in no small measure on the Nobel prize winning work of Herman Müller which showed a clear linearity between dose and induction of genetic mutations in fruit flies with no apparent threshold, and to 1959 testimony by Caltech geneticist E.B. Lewis, who proposed before Congress the ALARA protection philosophy based on genetic effects. Initially, the linear hypothesis was chosen because of its mathematical simplicity, and the fact that of all the dose response curve choices, it provided an *upper limit* on the risk to the exposed individual.

Largely within the past two decades, the linear, no-threshold model has assumed increasing regulatory importance and is now generally applied in radiation risk studies. In an effort to ensure the safety of the worker and the general public, evidence contradictory to a linear, no-threshold model is rejected out of hand by otherwise responsible scientists and regulators, leading to acceptance of the model as a fundamental law or paradigm, rather than as a hypothesis or theory. What we know (or should know) and bear in mind in our standards-setting process is that the linear, no-threshold hypothesis does not apply to all radiation dose responses, and that for some effects there may in fact be a threshold, or a nonlinear response.

History: The Linear, No-Threshold Model

David S. Gooden

The linear, no-threshold model for radiation injury evolved during the Cold War's era of intense above-the-ground testing of nuclear weapons. In the 1950s, ^{90}Sr and ^{137}Cs from fallout were known to exist in small amounts in milk and other foods. There was a fear that exposure to these and other radioactive materials would compromise our nation's genetic pool. This fear was based on the belief that genetic injury was a linear, no-threshold phenomenon. The belief was attributed to experimentation with the fruit fly (Drosophila). However, Dr. H.J. Müller, the Nobel Prize winner for genetic work with the fruit fly, said in his 1927 article that

> "while the figures are not quite conclusive, they make it probable that, within the limits used, the number of recessive lethals does not vary directly with x-ray energy absorbed, but more nearly with the square root of the latter...should this proportionality be confirmed, we should have to conclude that these mutations are not caused directly by a single quanta of x-ray energy that happens to be absorbed at some critical spot (emphasis added)" (Müller 1927).

This clearly is an early statement for *sublinearity*, not

linearity. The *UNSCEAR 1958 Report* claimed no genetic damage, even in the fruit fly, below what could be called a 25 rad threshold (UNSCEAR 1958). This value is within the range of other apparent "threshold" doses identified in other diseases such as radiogenic leukemia in the atomic bomb survivors (UNSCEAR 1994). Hereditary injury due to radiation exposure of humans has not been identified at all.

Also in the 1950s, a physician, E.B. Lewis, contributed to the belief in a linear, no-threshold paradigm for radiation injury. Lewis claimed that radiation-induced leukemia was a linear, no-threshold phenomenon. This is not the case (UNSCEAR 1994). It is now known that radiogenic hereditary injury and leukemia, the two premises on which the linear, no-threshold model was originally based, are not linear, no-threshold phenomena.

In spite of the loss of early foundations, the linear, no-threshold model continues to persist because once it was put into place, it was maintained by value systems (*science policy*), not science fact.* Through usage, the model became an article of faith and competing models of radiation injury were excluded from consideration. The model influences all of our radiation safety actions and all our related health and safety regulations. It is time to evaluate our science policy to see if it serves us well, based on our science facts.

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*L.A. Sagan, address to the **1992 International Conference on Low Dose Irradiation and Biological Defense Mechanisms, Kyoto, Japan.** Sagan noted that Thomas Kuhn, in his seminal work, **The Structure of Scientific Revolutions**, pointed out that most scientists are not seekers after truth, but rather are technicians who are taught to unquestioningly adopt certain models or paradigms. Their scientific endeavors, therefore, are limited to modifying only the details of the paradigms and the paradigms themselves are rarely challenged. Kuhn states that scientists "censor" information that is inconsistent with the paradigm. He believes that in the absence of concrete scientific findings the influence of personal and community values (which scientists share) contributes to the construction of paradigms.

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Changes in an Isolated Molecule Versus Human Health Effects

R.G. Thomas

There is little doubt that ionizing radiation will induce some change in an organic molecule. In other words, if one were to place an *in vitro* dish of biologically active molecules, say proteins, in the beam of a radiation source, and if measurement were made of all subtle changes in that molecule, then a radiobiological effect would be recorded on that molecule.

The common sense question that should follow such an event is: Does that subtle change in an isolated molecule have any relationship to some health effect in an irradiated person?

The linear extrapolation dogma is not based upon scientific or epidemiological evidence of radiation-induced health effects. We have a complicated system in the human body, complicated by all sorts of intricate machinery such as the immune system, designed to protect us.

Subtle molecular changes observed *in vitro* generally have no extrapolative powers to the human being because of the human repair process; they can only be scientifically based if proven to be related. Molecular biologists tend to show a radiation effect upon their favorite molecular or cellular system, with the implication that a related health effect should be considered in radiation protection criteria.

We know of no human cancer cases resulting from doses of radiation below at least 0.2 Gy (20 rad). Why are we worrying about what happens as zero dose is approached? Why are we sufficiently mentally insufficient to even consider guidance doses of 0.01 mSv (1 mrem) yr^{-1}, in the range where it cannot be measured?

If we are that concerned, what are we to do about natural background, which can vary by 1-3 mSv yr^{-1}, depending upon geography? (The frightful part of this latter is that some day, some person who considers him/herself an epidemiologist, is going to find some biologically related effect that is endemic to the people of Estes Park, Colorado, that is not found in Baltimore, Maryland, and the Press and the zero dose-zero effect people in our litigious society will eat it up.)

The plea here is for common sense. Is it ever going to be possible for influential people to recognize that an effect on a molecule, which may extrapolate linearly to the zero dose-zero effect point, is meaningless when it comes to setting standards for radiation, where no cancerous effects have been seen below rather sizeable doses? The answer unfortunately is no; there is too much job security and notoriety at stake.

The Cell Dose Approach Uncovers the Probability of a "Threshold" for Late Tissue Response at Exposures to Low Doses of Ionizing Radiation

Ludwig E. Feinendegen

Risk of detriment to biological systems from exposure to ionizing radiation is conventionally related to absorbed dose in the irradiated tissue.

This approach does not take into consideration the microscopic distribution of energy deposition events from tracks of ionizing particles (referred to here as hits) in tissue, nor does it relate to the multicellular structure of tissue.

Cells are the elemental units of life in tissue and respond as entire microorganisms, i.e. as a whole, to physiological or pathological interventions. Responses of hit cells underlie tissue detriment. Late effects, such as cancer and genetic mutations in germ cells with hereditable diseases in the offspring, arise from single cells.

At low values of absorbed dose or dose rate only single cells are hit per defined time interval, and the quantities of absorbed energy per cell (referred to here as cell doses, or hit sizes) conform to a spectrum that is typical for a given radiation quality.

At low-level exposure, absorbed dose to tissue thus is inadequate for assessing effects of radiation in hit cells potentially causing cancer or genetic mutations. The use of the relative biological effectiveness (RBE) or the quality factor of a radiation only partially corrects for the discrepancy between the values of absorbed dose to tissue and that to hit cells in that tissue when assessing risk from low-dose exposure (Feinendegen et al. 1994).

Individual cells in tissue respond in various ways to having been hit. According to experimental evidence, one response may lead to a permanent alteration in the DNA with the consequence of malignant transformation, with a probability of about 10^{-14} per x-ray hit (Feinendegen 1990).

Other responses may, with a probability closer to one, involve the cells in temporarily improving on the one hand their defense -- for example against metabolically produced aggressive oxygen-containing radicals (Feinendegen et al. 1987; Feinendegen et al. 1988; Hohn-Elkarim et al. 1990) -- and on the other hand their capacity of repair -- for example of DNA damages incurred from such radicals or other toxic agents (Wolff et al. 1988; Wolff 1992).

Also, hit cells may be induced to apoptosis and thus eliminate damages carried by them (Kondo 1993). Cells of the immune system have been reported to be stimulated, resulting in an improved surveillance in tissue against malignant cells or against potentially toxic agents (Makinodan 1992). The ratios of probabilities of some of these responses have been shown to change in favor of benefit with decreasing dose to the cells (Feinendegen et al. In Press).

The response of tissue to low-dose exposure must be viewed as a net consequence of multiple cellular responses in the irradiated tissue (Feinendegen 1991); the algebraic sum of cells that experience a temporary protection against spontaneous malignant transformation, and that, after malignant transformation, are eliminated by a stimulated immune system, may outweigh the sum of cells that sustain a radiation-induced malignant transformation at a given dose.

In view of the demonstrated increase of the ratio benefit to detriment in hit cells with decreasing dose to the cells, the relationship between probability of detriment in tissue and tissue-absorbed dose is predicted to deviate from linearity toward a "threshold" with decreasing doses.

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Dose, Response, and Biological Level

Charles A. Sondhaus

Is response a linear function of radiation dose, or must dose exceed a threshold to produce a response? This depends on how dose and response are specified. Organisms and their tissues are cell systems; both dose and response can be defined at either cell or tissue level. Conventionally measured, (absorbed) dose is the mean value of aggregate energy deposited in unit mass of tissue by many discrete ionizing events (hits). Each hit deposits a different amount of energy, and occurs randomly in individual cells. Microscopic dose in cell targets is highly variable; it does not equal the mean value until every cell is hit repeatedly (Booz and Feinendegen 1988).

At the low doses and dose rates from natural background or involved in protection, photon and secondary electron fluences do produce many events in each cell. However, most single photon events are not energetic enough to cause observable responses; to do so, multiple events must occur almost simultaneously in a given target. Conversely, equal doses from heavy charged particles or neutrons are distributions that include many events large enough to cause cell responses; however, few cells in the irradiated tissue are hit even once (Bond et al. 1988).

The probability of any cell response depends on event size. It remains very small for small hits, then increases rapidly and becomes quite high for large enough events, as shown by the "hit size effectiveness function (HSEF)" (Sondhaus et al. 1990). Yet few, if any, responses result unless single hits deposit enough energy to overcome free radical removal and DNA repair mechanisms (Feinendegen et al. In Press).

A given radiation produces the same relative distribution of single event sizes at any low dose level. The probability per unit fluence of causing a given cell response can be derived by convoluting this distribution with the HSEF. It differs, for example, by three orders of magnitude between ^{60}Co gamma photons and low-energy fast neutrons.

The number of aberrant cells that result from a given fluence of any radiation will thus increase linearly with increasing fluence, at least in the low-level region. However, appreciable numbers of responses will not begin to appear until the number of sufficiently energetic events exceeds some specific value. Accordingly, a dose level should exist below which the number of aberrant cells produced in an irradiated cell population remains so small that a functioning immune surveillance system may eliminate most, if not all, of them.

Thresholds may therefore occur on two levels: in cells, where single events may not deposit enough energy to cause responses, and in tissue, where the resulting number of aberrant cells may remain small enough to be controlled by the immune system. A level of irradiation should therefore exist below which no effects on tissues or organisms are expressed (Cronkite 1990).

There is evidence for the plausibility of this hypothesis. A prime example is the slow-but-successful evolution of complex organisms under the constant cosmic and terrestrial background irradiation that has existed throughout their long history on earth.

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The Linear, No-Threshold Model Fails Badly in the Low-Dose Region

Bernard L. Cohen

There is no experimental evidence for a linear, no-threshold dose-response relationship for radiation-induced cancer in the low dose, low-dose rate region of the vast majority of applications. (In this region, "linear-quadratic" reduces to "linear, no-threshold.")

The only basis is in this theory: a cancer is initiated by a single particle of radiation interacting with a single cell nucleus, so the cancer risk is proportional to the number of particles of radiation, which is just proportional to the dose. However, this very simple theory ignores the effects of repair processes which prevent the vast majority of initiating events from developing into cancers.

If the efficiency of these repair processes is affected by radiation, the simple theory obviously becomes invalid, and any reason for accepting a linear, no-threshold relationship collapses.

It is now indisputably clear that small doses of radiation do indeed affect the efficiency of repair processes. The best evidence for this is the "adaptive response" which is the topic of a forthcoming ICRP Report. Numerous papers on this are contained in Sugahara et al. 1992, and a brief review is given in Cohen 1994.

A typical result stated in one of these papers is that a 1 rem dose several hours before a 200 rem dose reduces the cancer risk from the latter by about 35 percent, which is

interpreted as an increase in production of repair enzymes by the 1 rem dose. Another supporting finding is that 1-5 rem of radiation strongly stimulates the immune system, which may also be protective against development of cancer.

Thus there is no evidence, experimental or theoretical, to support a linear, no-threshold relationship in the region of interest, and the only way to investigate it is through experiment. Unfortunately, traditional approaches to such investigations are very strongly inhibited by statistical problems. At least many tens of thousands of subjects would be required, and no such studies are in prospect.

However, an innovative approach to testing the linear, no-threshold relationship with no statistical limitations has recently been described in *Health Physics* (Cohen 1995). It utilizes an ecological approach, but it shows that "the ecological fallacy," which is the usual objection to ecological studies, is not applicable in this work.

It also addresses all other potential problems with ecological studies that have been discussed in the literature, and shows that they have little effect. It includes studies of potential confounding by 54 socioeconomic variables plus many climatic variables and geographical factors. The conclusion is that the linear, no-threshold theory fails very badly in the low-dose region, grossly overestimating the risk of low-level radiation. In the ten weeks since that paper appeared, no letters to the editor critiquing it have been received.

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Threshold Proven for High LET Radiation?

Carl H. Distenfeld

Professor Bernard Cohen, in his article *Relationship Between Exposure to Radon and Various Types of Cancer* (Cohen 1993), made the point that for linear, no-threshold dose effect response the ECOLOGICAL FALLACY DOES NOT APPLY. He first published this finding in the Int. J. Epidemiology (Cohen 1990).

If the ECOLOGICAL FALLACY does not apply, then the massive mortality and ecological data Cohen published is valid for risk estimation. Cohen's risk results show a negative relationship between environmental radon exposure and lung cancer, for either sex, with or without correction for smoking. Under the condition noted above, Cohen's work provides compelling statistical evidence for a threshold, if not a beneficial effect for high LET exposures of lung tissue at environmental levels.

What compelling evidence exists for linear, no-threshold effects? Should we continue to ignore the counter evidence and retain the linear, no-threshold extrapolations from acute high exposures? I believe it is past time to act on what we know, and I hope this may help reverse the morbidity of nuclear research, applications, and power.

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The Linear Hypothesis is Too Expensive

A.N. Tschaeche

The use of the linear hypothesis in setting radiation protection standards was appropriate 50 years ago. Now, we know much more about the actual harm that low levels of radiation DO NOT cause in humans. No peer-reviewed study to date demonstrates that annual doses on the order of 0.05 mSv (5 rem) per year cause significant harm to humans. Therefore, the linear hypothesis should no longer be used. Instead, a specific value such as 0.05 mSv (5 rem) per year should be the level below which no resources should be spent to further reduce the dose. Populations that receive such doses should be studied to verify that the level is appropriate to maintain safety.

The ICRP, NCRP, and EPA should use a philosophy for setting radiation protection standards that adopts a numerical value for annual dose below which regulatory agencies do not need to provide requirements and above which the process of ALARA is applied. That value should be 0.05 mSv (5 rem) per year for everyone (radiation workers and members of the public alike). Then the United States would not have to spend billions to save hypothetical lives. The public's fear of radiation should be alleviated. We could get on with radiological waste disposal. The United States would be more competitive in the world market. We could stop burning fossil fuels altogether by using hydrogen produced from nuclear-generated electricity to power autos and airplanes and by using nuclear-generated electricity for other things. All of those benefits can be ours if we only get rid of the very expensive linear hypothesis which is not fact. Deleting the linear hypothesis is an idea whose time has come.

The Deceptive Nature of a Dose-Based Statement of the Linear, No-Threshold Hypothesis

V.P. Bond

The following demonstration of the irrelevancy of a dose-based statement and "proof" of the "linear, no-threshold hypothesis," depends on making a sharp distinction between the amount of the radiation agent, the imparted energy, ϵ, in joules, and the average energy concentration, ϵ/m, the absorbed dose in Gy (Bond 1992; Bond et al. 1991).

With many biological systems -- e.g., cells in tissue culture -- one can easily adjust the numbers of cells used at all data points, in the range of about 0.7 Gy to perhaps several Gy, so that a clearly significant fraction of dosed cells will show a radiation-induced "quantal" response, e.g., malignant transformation, death. If that number of exposed cells is held constant and the absorbed dose is progressively reduced, a point is reached at which no significant excess is observable (Bond et al. 1995a).

This situation is frequently "remedied" by including more cells at that point to improve the statistical validity. However, because both axes are normalized, this data point, despite having gained statistical significance, remains at the same energy concentration (dose) value. This gives the false impression that no additional amount of energy is needed to achieve significance, at even the smallest doses.

However, if both coordinates are put in absolute terms, i.e., the number of quantal responses vs. the total amount of imparted energy, and the same exercise of "improving the statistics" is attempted, it then becomes evident that the point resulting from increasing the number of cells must be moved upward on the plot, to a substantially larger value. This exercise shows the irrelevancy of dose as the "amount" in articulating, or attempting to "prove," the "linear hypothesis" (Bond 1995b).

The fact that a proportionately larger population must be placed in the beam as the dose becomes smaller suggests that, for the production of an excess cancer, there must be a minimum average amount of imparted energy delivered to the population. This value, from human cancer epidemiological data and for penetrating photon radiations, is about 3 kJ (Bond et al. 1991). The above does not prove that, with small amounts of energy, the expectation value for cancer must be zero.

However, the extraordinarily large value for the average shows that the associated probability must be vanishingly small and of no public health significance. Accordingly, it is strongly recommended that the "linear hypothesis" be abandoned.

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It's Time for a Re-Examination

Andy Hull

The linear, no-threshold hypothesis was adopted by standards-setting groups in the mid-1950s. It was clearly stated at that time that it was adjudged to be a conservative assumption in the absence of any experimental evidence in the low dose, low dose-rate region. They stated that the true risk of genetic effects and, later in the 1960s, of cancer (as the Japanese data became available), might be much lower and even zero. Hormesis had not yet been proposed. At that time, the focus was primarily on workers and there was little, if any, attention paid to doses to the public much smaller than the 1/10 of the worker standards, which was the prevailing "public" upper limit standard.

With the advent of ICRP-22 and its principle of optimization, the collective dose and the man-rem (later the person-rem) became a consideration. At this time, there were serious proposals for a lower-limit cutoff in its calculation and for standards for the public either at the background level or its standard deviation (Adler and Weinberg 1978).

However, none was adopted and what was initially proposed as a conservative assumption has subsequently been adopted by regulatory agencies as a hard and fast basis for regulation, with calculations of hypothetical cancer deaths as low as less than one per year and comparisons of them with actual deaths from causes other than radiation by way of justifying their actions (EPA 1989).

When the linear hypothesis is used to justify regulation at extremely low levels and the resultant commitment of scarce resources to comply with regulations when the total number of cancer fatalities in this country is approximately 500,000 annually, it seems to me that it is time for its critical re-examination with the hope of steering resources toward more obvious causes of cancer and their alleviation.

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Discontinue Use of Linear Models

H. Wade Patterson

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It seems indisputable that the Linear Model(s) disagree with measured human response to radiation exposure and, as Richard Feynman put it, "If it disagrees with experiment it is wrong."

I therefore suggest that UNSCEAR, BEIR, ICRP, NCRP, EPA, and NRC discontinue their use of the Linear Model(s) for setting protection standards and for assessing risks from low-level exposures.

Radium Dial Painters Show A Practical Threshold

R.G. Thomas

It has been known for decades that data from the study of persons who had acquired body burdens of radium have shown no radiation-related bone cancers below some level of dose, often referred to as a practical threshold dose. This practical threshold concept was published by Evans et al. (1972) and followed more recently by Maletskos et al. (1992) and by Thomas (1994). The most conservative estimate of this threshold is 4 Gy to the average skeleton. There are over 1300 radium dial painters still alive and carrying skeletal doses upwards of 10 Gy who have not reported evidence of osteosarcomas.

What happens to the theories and practices of those who say that all radiation is harmful when cases like the radium dial painters appear? The perfect example of one way this has been handled is seen in the *Federal Register* (1991). The following is loosely quoted from this reference.

> The Scientific Advisory Board/Radiation Advisory Committee (SAB/RAC) urged EPA to base its risk assessment for radium on human epidemiology data on radium watch dial painters, rather than on modeled estimates, and urged EPA to present its rationale for adopting the modeling approach for radium risk assessment. The SAB/RAC also requested that EPA better describe its dosimetric model in the revised criteria document, including calculated doses and risk to organs, and that if EPA continued to use the modeling approach, uncertainties in the modeling be addressed.
>
> EPA REPLY: The Agency carefully reconsidered this issue. First it should be pointed out that all risk estimates are based on epidemiologic data and require mathematical modeling. The EPA uses the wealth of epidemiologic data on human exposure and risk of radiogenic cancers, including radium dial painters and

epidemiologic data on bone sarcomas resulting from injected ^{224}Ra.

The watch dial painter data indicate that the incidence of bone sarcomas may follow a dose-squared response, especially at higher exposures. **EPA policy, supported by recommendations of SAB/RAC, is to assess cancer risks from ionizing radiation as a linear response. Therefore, use of the dial painter data requires either deriving a linear risk coefficient from significantly non-linear exposure-response data, or abandoning EPA policy and SAB/RAC** advice in this case.

As a result of this interchange, the EPA uses data from the 3.6 day half life ^{224}Ra to establish some guidelines for 1500 year ^{226}Ra.

What about the radium threshold? Is it real? Isn't it interesting, the steps that will be taken to avoid reality?

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LNT Model Impacts NORM

Susan S. Mileti and Michael J. Kletter

The DuPont Minerals Business appreciates this opportunity to comment on the linear, no-threshold theory (LNT) for low-dose radiation. Our business manages naturally occurring radioactive materials (NORM) contained in our raw material mineral ores. The precedent of regulating NORM-containing minerals and wastes based upon the LNT could have a material impact on DuPont, and our small business minerals customers, as well as building construction, power plants, coal and ash storage sites, oil and gas, municipal drinking and wastewater plants, landfills, and incinerators. The 1994 UNSCEAR report adds significant scientific weight to the evidence opposing the LNT. Upon reinterpretation of the atom bomb survivor data, UNSCEAR concluded that the data could not be used for statistical verification of effects at low doses. In addition, the existence of hormesis is acknowledged.

There are additional studies which do not support the LNT, only a few of which are documented here. A comparison of Yangjiang County, China, with high natural background radiation, with two adjacent low-background counties showed that cancer mortality was lower in the high-background county (Wei et al. 1990). The BEIR V report states, "No increase in the frequency of cancer has been documented in populations residing in areas of high natural background radiation." It notes several studies where natural background gamma levels were three to four times normal (BEIR V 1990). Recent studies on the effect of indoor radon also throw doubt on the LNT, including a Chinese study measuring the radon level in the homes of women with and without lung cancer (Blot et al. 1990) and a study of nonsmoking Missouri women, selected so as to minimize the potentially confounding influence of cigarette smoking (Alavanja et al. 1994). Additional studies are referenced in the 1994 UNSCEAR report and in a paper by Zbigniew Jaworowski (Jaworowski 1995), a former chairman of UNSCEAR.

The HPS should urge the EPA, NRC, State Conference of Radiation Control Program directors, and state regulators to utilize their best Radiation Science Advisory Boards, ICRP, and NCRP to review the 1994 UNSCEAR report and other recent publications and encourage full scientific debate to consider all opposing data before imposing costly regulations based on the LNT. The LNT has been translated by the EPA and NRC to a 15 mrem yr^{-1} limit (draft 40 CFR 196, 40 CFR 193, and 59 FR 43200), and via precedent, what may likely be future regulation of NORM. This standard is too low, and for NORM equates to a cleanup of ^{226}Ra of 0.1 pCi g^{-1} for a residential site reuse or 0.3 pCi g^{-1} for commercial or industrial use, well within the normal background range of 1-5 pCi g^{-1} in soils.

The HPS should lead public understanding and acceptance of low-level radiation as part of life. Regulators should propose radiation regulations that are easily distinguished from background levels to alleviate public fear and misunderstanding of radiation. HPS can help EPA to avoid betrayal of public trust and backlash at over-regulation which is costly to society without benefit to public health.

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Radiation Hormesis for Health

T.D. Luckey

The Kobe catastrophe reminds us of our timorous existence on this planet. The bad news was the "unquenchable fires" from broken gas (the "clean fuel") lines, disruption of city infrastructures, destruction of homes, individual suffering, and over 5,000 deaths. The world sympathizes and will help rebuild Kobe.

Who will help avert the silent catastrophe which accounts for 10,000 premature deaths each week in the United States? At the November 1994 American Nuclear Society Meeting, John Cameron reviewed Matanoski's study showing a 24 percent decrease, $p<0.001$, in the death rate of white male workers with lifetime exposures >5 mSv (Matanoski 1991). This is a perennial health disaster. Matanoski's study and three studies which show significantly **reduced total cancer mortality rates** in exposed white male workers, a total of about seven million person-years, provide a powerful incentive for **radiation supplementation** as a public health service (Luckey 1994). Recent results from 15,727 Los Alamos National Laboratory workers support the same conclusion (Wiggs 1994). The use of control cohorts of unexposed workers in each plant negates the usual "healthy worker effect."

Extrapolate Matanoski's results to the total population of the United States, and you get 2,236,000 deaths per year (U.S. 1994). If our exposure to ionizing radiation were increased 1 mGy yr^{-1}, equivalent to that of many exposed nuclear workers, we could expect 537,000 fewer deaths per year attributable to a **partial radiation deficiency**.

Safe supplementation with ionizing radiation should be possible. Generations have lived with >20 mGy yr^{-1} (see Table). No health problems have been attributed to excess irradiation in these populations. Intensive animal studies on growth and development, reproduction, neurolomuscular activity, learning and memory, immune competence, infection and cancer mortality, and average life span show that chronic, whole-body exposures to low-dose irradiation is a biopositive force throughout ontogeny (Luckey 1991).

The decreased quality of life and the cost of this massive **premature illness and death** are devastating. These costs, plus the increased productivity of those 24 percent who died prematurely, would more than offset the costs of: 1) radiation supplementation and 2) quality care for the increased number of old people.

The hormesis model suggests a new plateau of health for the 21st century. If our exposure were doubled to 5 mGy yr^{-1}, the premature deaths prevented would be equivalent to a Kobe catastrophe every day. Also, a safe allowance for nuclear workers, 26 mGy yr^{-1} for 20 years, would help to restore our industrial health (Luckey In Press).

TABLE

Location	mGy yr^{-1}	Ratio
United States Average	2.6	1.0
Nile Delta	3.5	1.3
Exposed Workers[a]	3.6	1.4
Chernobyl Limit[b]	5	1.9
Proposed Allowance	5	1.9
Kerala India	4-13	3.5
Guarapari Brazil	10-18	5.4
Meaipe Brazil	22	8.5
Gerais Brazil	23	8.8
Kerala Beach	23	8.8
Proposed Worker Limit	26	10.0
Araxi Brazil	35	13.5
Optimum	100	38.5
Ramasari Iran	243	93.5
Guarapari Beach	263	101.2
The Zep[c]	10,000	3,850

a. This estimate includes natural plus industrial exposures.
b. The limit (in mSv) used to displace 200,000 persons.
c. The Zero Equivalent Point, this threshold dose is the limit of low-dose irradiation.

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The Low Dose Question

Harald H. Rossi

Dosimeters can measure the degree of compliance with dose limits but they give only a general indication of radiation risk unless the probability of deleterious effects is proportional to the absorbed dose (or dose equivalent). The dose registered by a dosimeter is the arithmetic sum of various increments regardless of when they were received. The "linear hypothesis" requires the same assumption with regard to effect probability (Rossi 1984).*

The desire to regard the dose as a direct measure of risk has at least influenced the choice of the linear model -- especially by organizations that promulgate radiation protection standards. This central tenet can be defended as long as epidemiological data cannot be considered to be in conflict with it. In view of the wide limits of confidence this has been -- and remains to be -- a mild restriction. It

has, nevertheless, become apparent that a "linear-quadratic" rather than a linear dependence on dose is a better approximation in the case of mortality from leukemia. The hope that one could salvage linearity at least at low doses is considerably dampened by a graph in the last report by UNSCEAR (UNSCEAR 1994) where any linear coefficient is negative and the "natural" mortality is reduced by doses of less than 0.2 Sv. The statistics for leukemia are optimal because the risk -- at least at high doses -- is relatively large and the expression time is relatively short; but various possible sources of error would make it unwise to conclude that a beneficial effect at low doses has been established.

It is, however, possible to claim this in several instances of animal carcinogenesis. "Hormesis" has been found in cases where the natural incidence is so high that a reduction at doses of the order of tenths of grays in carcinogenesis was distinctly identified.

Dose-effect curves for animal tumors also vary greatly in shape and this argues against the assertion that for solid human tumors they are simply straight lines of different slope. It is, nevertheless, not impossible that what are curves of various shapes for individual cancers could add up to something that approaches a straight line for all cancers. However, this should not be considered to be proven. Most of the data come from the studies of Japanese survivors of A-bombs. The neutron component has been incorrectly analyzed (Rossi and Zaider 1990) and while it had been considered to be of minor importance, this has recently been questioned. The relatively precise chromosome assays show the typical linear dependence for Hiroshima survivors and a linear-quadratic dependence for Nagasaki survivors (Stram et al 1993). This kind of difference indicates serious errors in the dosimetry on which these curves are based.

The epidemiological data which carry substantial uncertainties at all doses become essentially useless at doses of less than a tenth of a gray. Substantial extrapolations are required to evaluate the "risk" to radiation workers. They approach or exceed a factor of 100 when extended to such notions as the "risks" from background radiation or the "collective dose" received by populations. ICRP and NCRP can consider any projections to such levels to be quite safe because the "risks" are unmeasurable. However, in view of the complexity of the induction and the systemic responses in carcinogenesis such calculations are less than dubious.

*Assuming the usual case of low probabilities.

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It's Time to Re-Examine Our Dose-Response Model

Thomas F. McLeod
Thomas E. Boothe

Our current model to predict cancer induced by low-dose radiation is based upon a linear extrapolation with no threshold from populations exposed to high dose and high-dose rate radiation, a reasonable assumption if no direct measurements exist.

There are now an increasing number of studies designed to directly assess the incidence of cancer in populations exposed to low levels of radiation. Studies of radiation workers do not report excess cancers in this low dose, low-dose rate group. Our conclusion from these data is that the dose limits and accompanying radiation protection programs beginning in the 1950s must have been adequate since the incidence of cancer in these workers does not differ significantly from the unexposed population.

Epidemiological studies of cancer in populations exposed to low dose, low-dose rate radiation by living in high background areas have similarly not shown an increased incidence of cancer. The inhalation of high levels of radon is believed to cause cancer in underground miners but the risk to the general public has not been established and is inferred by extrapolation from the high dose using a linear, no-threshold model.

If this model is in fact correct, the postulated 15,000 lung cancer deaths per year in the United States attributable to radon (Samet 1994) should be detectable by epidemiological studies, even in the presence of the large number of uncertainties. The implication from these studies from three populations exposed to low-dose radiation is that radiation at these levels constitutes a very low risk or no risk.

An interesting observation by some studies (HBRRG 1980; Cohen 1995) is that the groups exposed to radiation appear to have fewer cancers. This puzzling observation, if in fact valid, might be explained by observations that a number of genes are inducible by heat, UV, and ionizing radiation and that this may be an adaptive response (Keyse 1993). While these *in vitro* studies cannot be interpreted as evidence for *in vivo* adaptation to radiation, they suggest that there may be a basis for a threshold.

In conclusion, the studies of populations exposed to low levels of radiation suggest there is no detectable effect (it may even be beneficial) in contradiction to predictions by extrapolation from high dose using a linear, no-threshold

model. We think that the low-dose studies are in several ways more compelling since they are looking for effects at exposure levels commonly encountered and hence it is time to re-examine our dose-response model in this light.

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Guidance Needed in Use of Models

Leonard R. Smith

Health physicists have long relied on expert committees to determine the best models for estimating the effects of low-level ionizing radiation. While this is appropriate, there is also a need for clearer guidance on how these models should be used. Some examples follow.

1. To assign detrimental effects to individuals or populations exposed to ionizing radiation it is necessary to measure those effects in a comparable population or to use a theoretical model to estimate effects.
2. We are currently unable to measure effects due to low doses and low-dose rates and we are also unable to test models proposed for extrapolating from observations at high doses.
3. It is good scientific practice to limit the use of models to estimate effects at doses that are within a factor of tens of doses where effects are quantifiably observed.
4. Measurements and estimates of radiation effects should be best estimates, not conservative estimates.
5. Estimates of radiation effects should be accompanied by specified uncertainties in the estimates including detrimental, zero, and protective effects, as appropriate.
6. Detrimental effects should not be assigned to an individual or population when the uncertainty in estimates or measurements greatly exceeds the magnitudes of the effects.
7. At our current level of understanding, quantitative assessments of detrimental effects can only be made with confidence for individuals who are exposed to doses approaching or exceeding current occupational dose limits.
8. Occupational dose limits and limits on exposure of emergency responders can and should be based on risk estimates and measurements. These radiation risks should be compared with the loss in life expectancy from other hazards in the work place.
9. Guidance on public dose limits and commonly experienced occupational dose require a different justification. An alternative, and preferable, method of justification is the ICRP 60 recommendation that public dose limits should be comparable with common variations in natural background radiation which are acceptable to the public.
10. The often repeated statement that it is "prudent to assume risk at any dose" is not correct when such action results in the abandonment of a beneficial practice involving radiation where there may be no risk, for an alternative practice where there is known risk.
11. It is prudent to consider the potential for risk at low doses. Guidance is needed on how to evaluate the significance of such potential risk.
12. It is very important that the NCRP and ICRP make best estimates of risk and clear recognition of the uncertainties. The tendency to default to conservative risk assessments could cause these organizations to be discredited in the event that future studies show that there is no risk at low doses.

Broad-Range Cooperative Study Needed

Bob Tuttle

We have seen many epidemiological studies on radiation dose effects that failed to achieve adequate statistical significance because the small effects at low doses require large populations. That deficiency has recently been attacked by the combination of studies on nuclear industry workers (Cardis et al. 1994) in which the records of nearly 96,000 nuclear industry workers were studied. This is a step in the right direction but, considering that the lowest dose range, just at and above natural background, currently creates the greatest economic, political, and technological impacts, it is still an inadequate step. Other occupationally exposed groups such as the Naval Shipyard Workers (Matanoski 1991) should be included, and so should the large public populations studied by the Massachusetts Division of Environmental Health Assessment (Morris and Knorr 1990) and by the National Cancer Institute (Jablon et al. 1990), as well as populations living in high natural background areas. Populations exposed in the former Soviet Union to military radioactive waste discharges and to the Chernobyl releases, and work done on radon exposures, should also be included. My point here is that the data set should be as comprehensive and complete as possible.

The data interpretation must accommodate a broad range in the quality of these data, and should be able to recognize

the apparent variety of beneficial, neutral, and detrimental health effects that results from various dose ranges, types of exposure, and forms of radiation. It is no longer adequate nor appropriate to only search for how harmful radiation exposure might be; the full range of effects must be considered. This interpretation must make sense of low, medium, and high exposures and single acute exposures, multiple acute (fractionated), chronic continuous, and chronic intermittent exposures, and must not simply throw away the "healthy worker" effect as a complication to the study. (An interesting reflection on the current DOE inquiry into the human radiation exposure experiments is that several "hopelessly ill" subjects were apparently saved by the radiation dose received experimentally, or perhaps they had been misdiagnosed? Their long survival after radiation exposure does not seem to have been identified as the result of "radiation-induced cures" Beardsley 1995).

Just such an integrated approach to data interpretation has been in use for the past 40 years or so in the interpretation of neutron cross-section measurements, which often produced data of greatly different quality, over broad, discrete, or limited energy ranges. This field of data interpretation has created many effective techniques and many associated practitioners, such as Charles Dunford at the National Nuclear Data Center at Brookhaven National Laboratory, Donald Smith at Argonne National Laboratory, and Francis Perey at Oak Ridge National Laboratory.

I think that a broad-range cooperative study, using the most complete set of data obtainable, interpreted by use of modern techniques, in an objective search for the most likely forms of radiation dose-response functions would be a most valuable investment for our future. However, I must add a pessimistic caution: the most influential government agencies in this field owe their current prosperity, in part, to public ignorance and fear of radiation, in the range of exposures where I propose we should search for truth. Because of this, funding, support, and even encouragement will be difficult to come by.

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Thyroid Cancer in the Low-Dose Domain

Ralph E. Lapp

The combination of high radiosensitivity and low incidence would appear to qualify a thyroid cancer epidemiology as the illuminator of the low-dose domain. In addition, the enhanced effect in infants would justify focusing on a very young cohort. A Swedish study (Lundell et al. 1994) of 14,351 infants under 14 months in age observed 17 thyroid cancers versus seven expected. A mean external irradiation of 27 rad was found, yielding a risk of 0.9 per million thyroid-rad-year (TRY).

To apply this risk to internal radiation from radioiodine, a factor of three reduces this risk to 0.3×10^{-6} TRY. This risk may be used to estimate the potential excess thyroid cancer among the very young milk consumers living near the Hanford nuclear site during the first years of plutonium production. A pilot study (Davis et al. 1995) of 3,200 children exposed to an ^{131}I dose of 11 rad has been endorsed by the National Research Council (1994). The collective dose of 35,000 thyroid-rad yields 1.1×10^{6} TRY. This results in a risk of 0.3 excess thyroid cancers for the CDC study. Such a radioiodine risk is not statistically sensible.

The prudence of the CDC (Davis et al. 1995) epidemiology needs to be examined by comparing its effective collective dose to that of the Swedish study (Lundell et al. 1994). The latter is 20-fold greater than the CDC study. A recent analysis of seven thyroid cancer studies shows no comparable epidemiology (Ron et al. 1995). Radiation-induced thyroid cancer in infants remains speculative. The CDC project (Davis et al. 1995) cannot illuminate the issue.

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Editor's Note: Scott Davis, Fred Hutchinson Cancer Research Center, is preparing a Hanford Thyroid Disease Study response to Ralph Lapp's article. It will be published in our July issue.

The Scientific Method and Radiation

Fritz A. Seiler

In the last few decades, efforts to model radiation risks have been carried out under the banner of scientific endeavors. On closer inspection, however, it becomes clear that these efforts were not guided by the scientific method. In fact, important aspects of these modeling efforts are in flagrant contradiction to some of the cornerstones of the scientific method.

An application of the six requirements of critical scientific thought (Lett 1990; Seiler 1994a), shows that the first, sufficiency, is fulfilled because there are sufficient data for a model in the low dose, low-dose-rate exposure regime of radiation protection. The second, replication, is met because there is enough evidence to confirm radiation carcinogenesis. The third requirement, however, is violated routinely, because not all the data available are included in the evaluations. In fact, some of the most pertinent data are ignored: data on cancer incidence in areas with different background doses. By the almost exclusive choice of A-bomb survivor data, we are led to believe that it is better to extrapolate cancer fatality data over six orders of magnitude in dose rate than to do careful evaluations of population doses accumulated at rates appropriate for the radiation protection of workers and the general population (Alvarez 1995).

The fourth requirement, that of a logical approach, is badly warped by regulatory policy. In the last decades, the question asked seems to have been "How do we keep the linear dose-effect relationship alive?" rather than "What do the data tell us?" The fifth, scientific honesty, has also suffered badly. In part, that requirement can be phrased as "What kind of scientific statement can we honestly make?" and here we are all at fault, mostly by keeping silent while regulations were discussed and promulgated which implied that we are able to measure, predict, and control risks with incredible accuracy, as accurate as 3×10^{-4} for some NRC regulations and 1×10^{-6} for NESHAPS. Recently, it has been shown that the situation is worse than expected, that the minimum significant radiation risk is as high as a few percent, and that there may be severe problems if we try to push it down toward 1×10^{-3} (Seiler 1994b).

The sixth, and often deemed the most important, requirement of the scientific method is falsifiability: the experimental testing of model predictions is of fundamental importance to the integrity of science. It is here, at low doses, that the linear model has failed decisively. At high-dose rates there is a threshold near a dose of about 0.3 Sv (Alvarez 1995; Shimizu 1993). Below that dose and its equivalent at low-dose rates, there is a region of hormesis, as demonstrated by Luckey (1991) and the 1994 UNSCEAR report (Jaworowski 1994). Once a scientific model has thus been falsified, the scientific method requires that it be abandoned and replaced (Seiler 1994a). It is our collective responsibility as scientists to see to it that the new model is constructed in strict adherence to the scientific method.

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Need for a New Model for Radiation Risk Assessment and Management

J.L. Alvarez

The linear-to-zero paradigm for radiation risk was initially introduced as an upper bound estimate for standard setting. It necessitates the introduction of concepts such as acceptable risk and "as low as reasonably achievable" but, above all, it is a model of convenience which has no basis in scientific fact. Nevertheless, it is touted at present as a dogma based on irrefutable fact. Two prestigious committees, BEIR 1990 and ICRP 1991, stated that the linear-to-zero model could neither be proven nor refuted, and that it was a biologically plausible model, although neither committee specified the properties which would make it linear to zero dose. In reality, there is no physical, chemical, or biological effect that has been shown to be linear down to zero dose.

This model has been disproved repeatedly in epidemiological studies involving radiation background and in radiation worker studies, but both committees dismiss all these studies as possibly confounded. However, their own data, the Japanese Atomic Bomb Survivor data, also refute the model in the low-dose region. In a paper submitted to *Health Physics* (Alvarez et al 1995), these data were examined for support of the linear-to-zero model and, at low doses, the data denied the existence of a carcinogenic effect, thus refuting the model. Several alternate models were examined and found to fit the data better than the linear-to-zero model. In all cases these were non-linear models with explicit or implicit thresholds. At high-dose

rates, the threshold was found to lie near 0.3 Sv. Further analysis showed that the model systematically overestimated the risk below 0.5 Sv, fulfilling the original intent of being an upper bound. Finally, no basis could be found for extending any high-dose rate model to low-dose rates.

These scientific deficiencies of the paradigm could be accommodated if there were a scientific method of managing risk. The major problems with the present way of managing risk are a lack of understanding of uncertainty and control, and a tendency to apply risk management to an isolated risk instead of all the risks involved (Seiler 1994a). Also, attempts to reduce risks, supported by a cost-benefit analysis, are doomed to failure due to the excessive conservatism in the evaluation of the risks. The lack of understanding of uncertainty and control arises mostly from not carrying uncertainties through the decision process and into the management of risk. This would lead to a minimum level of risk requiring action, which is completely analogous to minimum significant risk levels (Seiler 1994b). Above all, uncertainty restricts control: If the cancer rate is 0.25 ± 0.02, then risks of 0.001 ± 0.002 and lower do not alter an individual's cancer risk. Also, any effort to reduce a risk of 0.001 ± 0.002 must fail from lack of control.

Consequently, the current paradigm for radiation risk must be replaced by one which is scientifically defensible. Concurrently, risk management and control must be put on a scientifically valid basis.

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Radiation Protection is Not a Science at Low Doses

John Cameron

The statement by the National Council on Radiation Protection and Measurements (NCRP) that radiation risk may extend down to zero dose is quoted by many non-scientists (and some scientists) as though it had the same certainty as the laws of physics and chemistry. Biology at the human level is not a science. There are no quantitative laws similar to those of physics and chemistry. Even general health rules are subject to large variations. What is lethal for one person may have little effect on another.

This large biological variability has been known for centuries by medical practitioners. It is also well documented in the radiobiological literature. It led NCRP Scientific Committee 40 to conclude: "Because of the large range of RBE values for all endpoints reviewed, it must be a matter of judgment as to which values are to be used in selecting Q values for use in radiation protection" (NCRP 1990). Knowledge of Q (now W_R) values is necessary to calculate the basic radiation protection quantity *equivalent dose*. I was surprised when NCRP Report No. 116 (NCRP 1993) gave W_R values with no hint that they may not be valid. The reference for the values was ICRP Publication 60 (1991) while NCRP Report No. 104 was not referenced – it is a non report! However, NCRP still has confidence in its risk estimates. NCRP Report No. 115 (NCRP 1993) states that: "Finally, it should be noted that the current estimates provide a robust basis for radiation protection guidelines." This statement is one page after a list of five major sources of uncertainty in the risk factors, which does not include uncertainty in W_R values!

The most dramatic and convincing evidence of the failure of the linear, no-threshold assumption comes from the long-term study of radiation-induced osteogenic sarcoma in radium dial painters (Evans 1974). These data show a very large threshold of over 10 Gy of cumulative alpha particle dose to the skeleton for the radiation induction of bone cancer. If one uses a W_R (or Q) value for alpha radiation of 20, the threshold is over 200 Sv or 20,000 rem. Not only was the linear, no-threshold assumption contradicted but the stochastic model of cancer induction was strongly contradicted. Incidence of radiation-induced sarcoma was nearly independent of dose. Most of the women with cumulative skeletal doses over 250 Gy did not have osteogenic sarcomas. The general results of this important 1974 publication were recently confirmed (Rowland 1974).

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Appendix 4

ORIGINAL ARTICLE

Mortality among a cohort of uranium mill workers: an update

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Aims: To evaluate the mortality experience of 1484 men employed in seven uranium mills in the Colorado Plateau for at least one year on or after 1 January 1940.

Methods: Vital status was updated through 1998, and life table analyses were conducted.

Results: Mortality from all causes and all cancers was less than expected based on US mortality rates. A statistically significant increase in non-malignant respiratory disease mortality and non-significant increases in mortality from lymphatic and haematopoietic malignancies other than leukaemia, lung cancer, and chronic renal disease were observed. The excess in lymphatic and haematopoietic cancer mortality was due to an increase in mortality from lymphosarcoma and reticulosarcoma and Hodgkin's disease. Within the category of non-malignant respiratory disease, mortality from emphysema and pneumoconioses and other respiratory disease was increased. Mortality from lung cancer and emphysema was higher among workers hired prior to 1955 when exposures to uranium, silica, and vanadium were presumably higher. Mortality from these causes of death did not increase with employment duration.

Conclusions: Although the observed excesses were consistent with our a priori hypotheses, positive trends with employment duration were not observed. Limitations included the small cohort size and limited power to detect a moderately increased risk for some outcomes of interest, the inability to estimate individual exposures, and the lack of smoking data. Because of these limitations, firm conclusions about the relation of the observed excesses in mortality and mill exposures are not possible.

In the United States, mining and milling of uranium ores to recover uranium for nuclear weapons began during World War II to support the Manhattan Project. Uranium bearing ores had been mined previously on a small scale, but mainly for the recovery of vanadium. Continued development and expansion of the industry after the war was promoted by a domestic uranium concentrate procurement programme that was established by the Atomic Energy Commission in 1947.[1] As early as 1949, health officials became concerned about the potential health risks associated with uranium mining and milling.[2]

The health risks associated with uranium mining have been extensively studied. Uranium miners have been found to have a substantially increased risk of death from lung cancer, which is associated with cumulative exposure to radon decay products.[3–5] Excess mortality from non-malignant respiratory diseases has also been found.[6] However, existing data concerning the health effects of uranium milling are limited. Waxweiler and colleagues reported a significantly increased risk of "other non-malignant respiratory disease" (standardised mortality ratio (SMR) = 2.50; observed (obs) = 39) among 2002 workers at seven uranium mills in the Colorado Plateau.[7] This category included emphysema, fibrosis, silicosis, and chronic obstructive pulmonary disease. Non-significant excesses were observed for lymphatic and haematopoietic malignancies other than leukaemia after 20 years latency (SMR = 2.3; obs = 6) and chronic renal disease (SMR = 1.67; obs = 6). In an earlier overlapping study of 662 uranium mill workers, Archer and colleagues observed an excess risk of mortality from lymphatic and haematopoietic malignancies other than leukaemia (SMR = 3.92; obs = 4).[8] Limited data from morbidity studies suggest that uranium millers may have an increased risk of pulmonary fibrosis[2] and renal tubular injury.[9]

The primary exposures of interest in uranium mills are uranium, silica, and vanadium containing dusts. Inhalation of uranium dust may pose an internal radiation hazard as well as the potential for chemical toxicity. High concentrations of radon and radon decay products, similar to the levels found in underground uranium mines, are not expected in the mills.

Because of continuing concern about the health effects of uranium milling, we extended the follow up of the cohort described by Waxweiler and colleagues.[7] The present report describes the mortality experience of the cohort through 21 additional years of observation. In addition, the risk of end stage renal disease was evaluated among the cohort.

Uranium milling process

The primary function of uranium mills is to extract and concentrate uranium from uranium containing ore to produce a semi-refined product known as yellowcake. Yellowcake is a chemically complex mixture of diuranates, basic uranyl sulphate, and hydrated uranium oxides that contains 80–96% uranium as U_3O_8, UO_3, and/or ammonium diuranate.[10] Yellowcake is used commercially to manufacture nuclear fuel for nuclear power and national defence purposes.

Conventional mills process uranium bearing ores from underground or open-pit mines. Until the mid-1970s, all yellowcake in the United States was produced at conventional uranium mills.[11] The main stages of the process in conventional mills involved: (1) ore handling and preparation; (2) extraction; (3) concentration and purification; and (4) precipitation, drying, and packaging. So-called "upgrader" facilities processed virgin ore that was initially too low in uranium content to process economically in a uranium mill. At an upgrader, a series of crushing, grinding, and chemical separation steps were employed to "upgrade" the percent

Main messages

- Potential exposures among uranium mill workers that may be associated with adverse health effects include uranium, silica, and vanadium containing dusts.
- We observed a statistically significant increase in mortality from non-malignant respiratory disease and non-significant increases in mortality from lymphatic and haematopoietic malignancies other than leukaemia, lung cancer, and chronic renal disease. These findings were consistent with our a priori hypotheses.
- The SMRs for lung cancer and emphysema among men hired before 1955, when exposures to uranium, silica, and vanadium were presumably higher, were significantly increased and greater than the SMRs observed among men hired in 1955 or later. However, mortality for causes of death observed to be in excess did not increase with employment duration.
- Limitations include a lack of smoking data, small cohort size and limited power to detect a moderately increased risk for some outcomes of interest, and the inability to estimate individual exposures to uranium, silica, and vanadium.

uranium contained in the final product, which was sent to a uranium mill for further processing. Unlike conventional uranium mills, upgrader facilities did not carry out concentration and purification of the uranium, and precipitation, drying, and packaging of yellowcake. In this paper, the term "mill" will be used in reference to both conventional uranium mills and upgrader facilities.

METHODS

Cohort description

The cohort was assembled from the personnel records obtained from the companies operating seven uranium mills (five conventional uranium mills and two upgraders). The original cohort described by Waxweiler and colleagues, which is referred to hereafter as the Waxweiler cohort, included 2002 men who had worked for at least one day after 1 January 1940, worked for at least one year in uranium mills, and never worked in underground uranium mines.[7] Because some of the work histories in the Waxweiler cohort were found to be coded inaccurately, we recoded all work histories. We also reviewed documentation from the original study to identify men who met the original cohort criteria, but had been omitted. Personnel records were obtained and work histories updated for cohort members who were still employed in 1971 when the personnel records were originally microfilmed. After re-coding the work histories, we limited the cohort to men who met the original cohort criteria, had never worked in an above-ground or underground uranium mine, and had worked for at least one year in the seven uranium mills before the personnel records were originally microfilmed in 1971 while the mills were operating to recover uranium and/or vanadium concentrates. The final cohort included 1485 men, 1438 (96.8%) of whom were in the Waxweiler cohort. Of the 564 workers not included in the current study, 103 (18.3%) worked in uranium mines, 318 (56.4%) never worked in one of the seven mills comprising the study, 141 (25.0%) worked for less than one year in the seven mills when they were operating, and one (0.2%) was excluded because the work history was incomplete. One woman whose gender was coded incorrectly in the Waxweiler cohort was also excluded.

Follow up

The vital status of all persons in the cohort was determined until 31 December 1998. Follow up included inquiry through the Social Security Administration, Internal Revenue Service, US Postal Service, National Death Index (NDI), and state bureaus of motor vehicles. Death certificates were obtained from state vital records offices for some deceased members of the cohort and coded by a trained nosologist according to the revision of the International Classification of Diseases in effect at the time of death. The causes of death for other deceased members of the cohort were obtained from the NDI.

To identify cohort members with treated end stage renal disease, the cohort was linked with the End Stage Renal Disease (ESRD) Program Management and Medical Information System (PMMIS) by name, social security number, and date of birth. The ESRD PMMIS is maintained by the Health Care Financing Administration (HCFA) and includes all individuals who received Medicare covered renal replacement therapy (dialysis or transplant) in 1977 or later. Approximately 93% of ESRD patients in the United States are included in the ESRD PMMIS.[12]

Analysis

The mortality experience of the cohort was analysed with the use of the National Institute for Occupational Safety and Health (NIOSH) modified life table analysis system (LTAS).[13 14] Each cohort member accumulated person-years at risk (PYAR) for each year of life after 1 January 1940 or completion of the one year eligibility period, whichever was later, until the date of death for deceased cohort members, the date last observed for persons lost to follow up, or the ending date of the study (31 December 1998) for cohort members known to be alive. Cohort members known to be alive after 1 January 1979 (the date that the NDI began) and not identified as deceased were assumed to be alive as of 31 December 1998. The PYAR were stratified into five year intervals by age and calendar time and were then multiplied by the appropriate US gender, race, and cause specific mortality rates to calculate the expected number of deaths for that stratum. The resulting expected numbers were summed across strata to obtain cause specific and total expected number of deaths. The ratio of observed to expected number of deaths was expressed as the standardised mortality ratio (SMR). Ninety five per cent confidence intervals (CI) were computed for the SMRs assuming a Poisson distribution for observed deaths. The mortality analysis was repeated using Colorado, New Mexico, Arizona, and Utah state mortality rates to generate expected numbers of deaths. In addition to analyses of underlying cause of death, all causes listed on the death certificate were analysed using multiple cause mortality methods described by Steenland and colleagues.[15] Multiple cause analyses are particularly important for diseases that may be prevalent at death but that are not the underlying cause of death.[15] In analyses using state or multiple cause mortality rates, person-years at risk started to accumulate on 1 January 1960, when the rates were first available, or completion of the one year eligibility period, whichever was later.

The end stage renal disease experience of the cohort was analysed using methods described by Calvert and colleagues.[16] Briefly, the modified life table analysis system was used to calculate PYAR, expected number of individuals developing ESRD, and standardised incidence ratios (SIRs) for ESRD. Since the ESRD PMMIS is considered incomplete prior to 1977, cohort members who died before this date were excluded from the ESRD analysis. PYAR for cohort members

who were alive on 1 January 1977 began to accumulate on this date. Cohort members accumulated PYAR until the first service date for those with ESRD, the date of death for deceased cohort members, the date last observed for those lost to follow up, or the ending date of the study for those known to be alive. The first service date for ESRD, which generally represents the date on which renal replacement therapy began, was used as a surrogate for the date of onset of ESRD. After the PYAR were stratified into five year intervals by age and calendar time, the PYAR were multiplied by the appropriate US ESRD incidence rates to calculate the expected number of cases for that stratum. The US incidence rates were developed by NIOSH from the HCFA PMMIS data and US census data as described elsewhere.[16] The expected number of treated ESRD cases in all strata were summed to yield the total expected number. The ratio of the observed to expected number of treated ESRD cases was expressed as the standardised incidence ratio (SIR). The SIR for four major categories of ESRD (systemic, non-systemic, other, and unknown) were also calculated.

We stratified SMRs and SIRs by duration of employment (1–2, 3–9, 10+ years), time since first employment (latency) (0–9, 10–19, 20+ years), and year of first employment (<1955, 1955+). In general, the cut points for duration of employment and time since first employment were retained from the original study; however, we lowered the cut point between the lowest and middle duration of employment categories so that the number of deaths in each category would be more similar. The cut point for year first employed was selected a priori based on the assumption that exposures in the earlier years (when there was little emphasis on dust control) would be higher than in later years. Duration of employment was based on employment in the seven cohort mills while they were operating to produce uranium and/or vanadium concentrates and included employment that occurred prior to the start of the follow up period. The analyses were repeated restricting the cohort to those who had worked in a conventional mill and to those who had worked in a conventional mill that produced both vanadium and uranium concentrates. Because of the potential impact of exposures encountered during other employment in the uranium industry, SMRs and SIRs were also conducted restricting the cohort to those without such employment. All analyses were done using the PC version of the LTAS[17] (http://www.cdc.gov/niosh/ltindex.html). Testing for heterogeneity and trend in the SMRs used the methods of Breslow and Day.[18]

Based on previous studies and the known toxic effects of uranium and silica, the a priori outcomes of interest in this study included non-malignant respiratory disease, chronic renal disease, lung cancer, and lymphatic and haematopoietic cancer other than leukaemia. Within the major category of non-malignant respiratory disease, the minor category "pneumoconiosis and other respiratory diseases" was of a priori interest.

RESULTS

A total of 1484 men contributing 49 925 person-years were included in the study. Table 1 presents the distribution of the cohort by vital status, plant type (conventional mill, upgrader), duration of employment, time since first employment, and first year of employment. Race was unknown for 642 (43.3%) members of the cohort. Because all workers of known race were white, workers of unknown race were classified as white in the analysis. In the total cohort, 656 (44.2%) men were alive, 810 (54.6%) were deceased, and 18 (1.2%) were lost to follow up. Causes of death were obtained from death certificates or the NDI for 794 (98.0%) of the individuals known to be deceased. Deaths with missing causes of death were included in the other and unknown causes category. The duration of employment of the cohort is relatively short with a median of 3.6 (range 1–36.3) years. Over half of the cohort was first employed prior to 1955. The median time since first employment, based on employment in the seven mills while they were operating, is 37 years.

Table 1 Characteristics of the study population

No. of workers	1485
Excluded from analysis*	1
Person-years at risk	49925
Mill type	
Conventional mill only	1412 (95.1%)
Upgrader only	44 (3.0%)
Both	28 (1.9%)
Vital status as of 31 Dec 1998	
Alive	656 (44.2%)
Dead	810 (54.6%)
Unknown	18 (1.2%)
Year of birth	1921 median
	1872–1951 range
Year of first employment†	
Prior to 1955	799 (53.8%)
1955 or later	685 (46.2%)
Duration of employment†	
1–2 years	634 (42.7%)
3–9 years	547 (36.9%)
10 + years	303 (20.4%)
Time since first employment†	
<10 years	76 (5.1%)
10–19 years	128 (8.6%)
20+ years	1280 (86.3%)

*Missing date of birth.
†Employment in the seven mills while operating to produce uranium and/or vanadium concentrates.

Almost all of the workers and person-years were from conventional uranium mills. Of the 1440 men who were employed at conventional mills, 1263 (87.7%) were employed at mills that recovered vanadium, 145 (10.1%) were employed at mills that did not recover vanadium, and 32 (2.2%) were employed both at mills that recovered vanadium and mills that did not recover vanadium. Among the entire cohort, 83 (5.6%) men had also been employed in other aspects of the uranium industry according to their employment application or other employment records.

Table 2 shows the results of the analysis for all causes of death. Mortality from all causes was less than expected, which is largely accounted for by fewer deaths from heart disease than expected. Mortality from all malignant neoplasms was also less than expected. Among the outcomes of a priori interest, a statistically significant increase in mortality from non-malignant respiratory disease (SMR = 1.43; 95% CI 1.16 to 1.73; obs = 100) and non-significant increases in mortality from trachea, bronchus, and lung cancer (SMR = 1.13; 95% CI 0.89 to 1.41; obs = 78), lymphatic and haematopoietic malignancies other than leukaemia (SMR = 1.44; 95% CI 0.83 to 2.35; obs = 16), and chronic renal disease (SMR = 1.35; 95% CI 0.58 to 2.67; obs = 8) were observed. The excess in mortality from lymphatic and haematopoietic malignancies was due to an excess in mortality from lymphosarcoma and reticulosarcoma (SMR = 1.74; 95% CI 0.48 to 4.46; obs = 4) and Hodgkin's disease (SMR = 3.30; 95% CI 0.90 to 8.43; obs = 4). Within the major category of non-malignant respiratory disease, mortality from emphysema (SMR = 1.96; 95% CI 1.21 to 2.99; obs = 21) and pneumoconioses and other respiratory disease (SMR = 1.68; 95% CI 1.26 to 2.21; obs = 52) was significantly increased. Among outcomes other than those of a priori interest, non-significant increases in mortality from other and unspecified cancers (SMR = 1.59; 95% CI 0.98 to 2.43; obs = 21) and accidents (SMR = 1.26; 95% CI 0.93 to 1.68;

Table 2 Uranium mill workers' mortality (since 1940, US referent rates): update of cohort to 1998

Underlying cause of death (ICD9 code)*	Obs	Exp	SMR	95% CI
All causes	810	877.66	0.92‡	0.86 to 0.99
All cancers (140–208)	184	204.12	0.90	0.78 to 1.04
Buccal and pharyngeal CA (140–149)	2	5.06	0.40	0.05 to 1.43
All digestive CA (150–159)	33	53.18	0.62§	0.43 to 0.87
Oesophagus (150)	1	5.06	0.20	0.01 to 1.10
Colon (152–153)	12	18.96	0.63	0.33 to 1.11
Rectal (154)	2	4.77	0.42	0.05 to 1.51
Liver and biliary (155–156)	4	5.04	0.79	0.22 to 2.03
Pancreas (157)	6	10.30	0.58	0.21 to 1.27
All respiratory CA (160–165)	78	72.29	1.08	0.85 to 1.35
Trachea, bronchus, and lung (162)	78	68.93	1.13	0.89 to 1.41
Male genital CA (185–187)	15	19.67	0.76	0.43 to 1.26
All urinary CA (188–189)	5	11.03	0.45	0.15 to 1.06
Kidney (189.0–189.2)	4	4.96	0.81	0.22 to 2.06
Leukaemia/aleukaemia (204–208)	5	7.62	0.66	0.21 to 1.53
Lymphatic and haematopoietic CA other than leukaemia (200–203)	16	11.08	1.44	0.83 to 2.35
Lymphosarcoma and reticulosarcoma (200)	4	2.29	1.74	0.48 to 4.46
Hodgkin's disease (201)	4	1.21	3.30	0.90 to 8.43
Other lymphatic and haematopoietic CA (202–203)	8	7.57	1.06	0.46 to 2.08
Other/unspecified CA (194–199)	21	13.20	1.59	0.98 to 2.43
Tuberculosis (001–008)	2	3.88	0.52	0.06 to 1.86
Diabetes mellitus (250)	10	14.60	0.68	0.33 to 1.26
Heart disease (390–398, 402, 404, 410–414, 420–429)	293	349.10	0.84§	0.75 to 0.94
Ischemic heart disease (410–414)	236	280.07	0.84§	0.74 to 0.96
Other circulatory disease (401, 403, 405, 415–417, 430–459)	69	83.06	0.83	0.65 to 1.05
Non-malignant respiratory disease (460–519)	100	70.16	1.43§	1.16 to 1.73
Pneumonia (480–486)	25	23.76	1.05	0.68 to 1.55
Chronic and unspecified bronchitis (490–491)	2	2.20	0.91	0.11 to 3.28
Emphysema (492)	21	10.72	1.96§	1.21 to 2.99
Pneumoconioses and other respiratory disease (470–478, 494–519)	52	30.87	1.68§	1.26 to 2.21
Non-malignant digestive disease (520–579)	23	36.91	0.62‡	0.39 to 0.94
Non-malignant genitourinary disease (580–629)	13	13.03	1.00	0.53 to 1.71
Acute renal disease (580–581, 584)	1	1.16	0.86	0.02 to 4.79
Chronic renal disease (582–583, 585–587)	8	5.91	1.35	0.58 to 2.67
Ill defined conditions (780–796, 798–799)	4	8.01	0.50	0.14 to 1.28
Accidents (E800–E949)	47	37.23	1.26	0.93 to 1.68
Violence (E950–E978)	18	17.73	1.02	0.60 to 1.60
Suicide (E950–E959)	15	14.19	1.06	0.59 to 1.74
Homicide (E960–E978)	3	3.54	0.85	0.18 to 2.48
Other and unknown causes	27†	14.04	1.92§	1.27 to 2.80

*International Classification of Disease codes, 9th revision.
†Includes 16 observed deaths with missing death certificates.
‡95% confidence interval excludes the null value (1.0).
§99% confidence interval excludes the null value (1.0).

obs = 47) were observed. The observed other and unspecified cancers were metastatic cancers of unknown primary site. Mortality from all digestive cancers was significantly less than expected (SMR = 0.62; 95% CI 0.43 to 0.87; obs = 33).

An analysis was also conducted (not shown) using US rate files for 1960 to 1999 which have 99 causes of death instead of 92 because these rate files include more detailed categories of non-malignant respiratory disease and slightly different categories of malignancies of the lymphatic and haematopoietic system. Of the 1484 cohort members, 89 (6.0%) were not included in this analysis because they had either died or were lost to follow up before 1960. Only one death from silicosis (SMR = 5.93; 95% CI 0.15 to 32.94) and two deaths from pneumoconioses other than silicosis and asbestosis (SMR = 2.29; 95% CI 0.28 to 8.25) were observed. The remainder of the excess in non-malignant respiratory disease mortality was due to a significant excess in mortality from emphysema (SMR = 1.83; 95% CI 1.10 to 2.86) and other respiratory diseases (SMR = 1.62; 95% CI 1.19 to 2.15). Most of the observed deaths from other respiratory diseases were due to chronic obstructive lung disease. In the category of malignancies of the lymphatic and haematopoietic system other than leukaemia, mortality was significantly increased for Hodgkin's disease (SMR = 4.01; 95% CI 1.09 to 10.25, obs = 4) and non-significantly increased for non-Hodgkin's lymphoma (SMR = 1.25; 95% CI 0.54 to 2.46; obs = 8).

In order to evaluate whether regional variations in mortality rates could explain the findings, analyses were conducted using state rates as the comparison population (table 3). State rates are not available before 1960 so men who had either died or were lost to follow up before 1960 were also excluded from this analysis. The excess in mortality from cancer of the trachea, bronchus, and lung (SMR = 1.51; 95% CI 1.19 to 1.89) based on state rates was statistically significant and greater than the excess based on US rates since 1960 (SMR = 1.13; 95% CI 0.89 to 1.42). In contrast, the excess in mortality from emphysema (SMR = 1.25; 95% CI 0.75 to 1.95) and other respiratory diseases (SMR = 1.35; 95% CI 0.99 to 1.79) was less than the excess based on US rates. Mortality from chronic renal disease was not increased based on state rates (SMR = 1.02; 95% CI 0.33 to 2.39; obs = 5) and was similar to that based on US rates since 1960 (SMR = 1.00; 95% CI 0.32 to 2.35). This is in contrast to the excess in mortality from chronic renal disease observed based on US rates since 1940.

Tables 4 and 5 show mortality according to duration of employment and time since first employment for selected causes of death based on US rates. Overall mortality was highest among those with the shortest duration of employment and lowest among those with the longest duration of employment. Similar trends with duration of employment were observed for mortality from lung cancer, non-malignant

Table 3 Uranium mill workers' mortality (since 1960) from selected causes of death (state referent rates): update of cohort to 1998

Underlying cause of death (ICD9 code)*	Obs	Exp	SMR	95% CI
All respiratory CA (160–165)	75	51.98	1.44‡	1.13 to 1.81
Trachea, bronchus, and lung (162)	75	49.73	1.51‡	1.19 to 1.89
Leukaemia/aleukaemia (204–208)	5	6.51	0.77	0.25 to 1.80
Lymphatic and haematopoietic CA other than leukaemia (200–203)	15	9.58	1.57	0.88 to 2.58
Non-Hodgkin's lymphoma (200, 202)	8	5.71	1.40	0.60 to 2.76
Hodgkin's disease (201)	4	0.94	4.24†	1.15 to 10.84
Myeloma (203)	3	2.93	1.02	0.21 to 3.00
Other/unspecified CA (187, 194–199)	22	11.93	1.84‡	1.16 to 2.79
Non-malignant respiratory diseases (460–519)	94	79.32	1.19	0.96 to 1.45
Chronic and unspecified bronchitis (490–491)	1	2.74	0.36	0.01 to 2.03
Emphysema (492)	19	15.22	1.25	0.75 to 1.95
Asbestosis (501)	0	0.12	0.00	0.00 to 30.62
Silicosis (502)	1	0.45	2.22	0.06 to 12.36
Other pneumoconioses (500, 503, 505)	2	0.40	5.04	0.61 to 18.19
Other respiratory diseases (470–478, 494–499, 504, 506–519)	47	34.86	1.35	0.99 to 1.79
Non-malignant genitourinary disease (580–629)	10	10.51	0.95	0.46 to 1.75
Acute renal disease (580–581, 584)	1	0.79	1.26	0.03 to 6.99
Chronic renal disease (582–583, 585–587)	5	4.89	1.02	0.33 to 2.39

*International Classification of Disease codes, 9th revision.
†95% confidence interval excludes the null value (1.0).
‡99% confidence interval excludes the null value (1.0).

respiratory disease, and emphysema. A positive trend between mortality and duration of employment was not observed for any of the selected causes of death except other and unspecified cancers. The excess in mortality from Hodgkin's disease was confined to 20 years or more since first employment. Mortality from Hodgkin's disease was significantly increased over sevenfold among this group, but the confidence interval around the point estimate was wide (95% CI 1.96 to 18.40).

Mortality was also examined (not shown) by date of hire (pre-1955 versus 1955 or later). There appeared to be a relation between an earlier date of hire and increased mortality from trachea, bronchus, and lung cancer (prior to 1955: SMR = 1.34, 95% CI 1.02 to 1.74; 1955 or later: SMR = 0.79, 95% CI 0.49 to 1.21). Mortality from emphysema was also higher among men hired prior to 1955 (SMR = 2.22; 95% CI 1.29 to 3.56; obs = 17) than among men hired in 1955 or later (SMR = 1.30; 95% CI 0.36 to 3.33; obs = 4), but mortality from pneumoconiosis and other respiratory disease was similar among men hired prior to 1955 (SMR = 1.69; 95% CI 1.17 to 2.36) and men hired in 1955 or later (SMR = 1.68; 95% CI 0.99 to 2.65).

Analyses of multiple causes of death and end stage renal disease incidence were conducted to further evaluate the risk of renal disease among the cohort. The risk of chronic renal disease mortality was not increased (SMR = 1.05; 95% CI 0.69 to 1.54, obs = 26) in the multiple causes of death analysis. The risk of treated end stage renal disease was less than expected overall (SIR = 0.71; 95% CI 0.26 to 1.55, obs = 6). The risk of treated end stage renal disease of unknown aetiology was increased (SIR = 2.73; 95% CI 0.56 to 7.98, obs = 3). This finding was based on three observed cases and the confidence interval was wide. The primary cause of renal failure was missing in the ESRD PMMIS for two of the three observed cases, raising the possibility that these cases were misclassified. Death certificates were available for these cases; renal disease was mentioned on the death certificate for both, but not a specific type or aetiology of renal disease.

Similar results were obtained when the cohort was restricted to men who were employed in conventional mills and when the cohort was restricted to men who were employed in conventional mills that produced both uranium and vanadium concentrates. Results were also similar when

Table 4 Uranium mill workers' mortality (since 1940) from selected causes of death by duration of employment (US referent rates): update of cohort to 1998

	Duration of employment (years)			
Underlying cause of death	1–2 SMR (obs)	3–9 SMR (obs)	⩾10 SMR (obs)	
All deaths	1.01 (352)	0.91 (295)	0.80 (163)†	‡
All cancers	0.94 (75)	0.91 (68)	0.83 (41)	
Trachea, bronchus, and lung CA	1.35 (36)	1.27 (32)	0.58 (10)	‡
Lymphatic and haematopoietic CA other than leukaemia	1.38 (6)	1.22 (5)	1.90 (5)	
Lymphosarcoma and reticulosarcoma	2.15 (2)	1.15 (1)	2.03 (1)	
Hodgkin's disease	1.91 (1)	4.25 (2)	4.57 (1)	
Other lymphatic and haematopoietic CA	1.03 (3)	0.73 (2)	1.56 (3)	
Other/unspecified CA	1.16 (6)	1.65 (8)	2.19 (7)	
Non-malignant respiratory disease	1.99 (53)†	1.12 (29)	1.02 (18)	‡
Emphysema	2.69 (11)†	1.79 (7)	1.11 (3)	
Pneumoconioses and other respiratory diseases	2.53 (29)†	1.07 (12)	1.35 (11)	
Chronic renal disease	1.27 (3)	1.33 (3)	1.53 (2)	

*95% confidence interval excludes the null value (1.0).
†99% confidence interval excludes the null value (1.0).
‡Test for trend p value <0.05.

Table 5 Uranium mill workers' mortality (since 1940) from selected causes of death by length of time since first employment (US referent rates): update of cohort to 1998

Underlying cause of death	Time since first employment (years)		
	<10 SMR (obs)	10–19 SMR (obs)	≥20 SMR (obs)
All deaths	0.95 (68)	0.87 (125)	0.93 (617)
All cancers	0.62 (7)	0.88 (25)	0.92 (152)
Trachea, bronchus, and lung CA	0.36 (1)	1.45 (13)	1.12 (64)
Lymphatic and haematopoietic CA other than leukaemia	1.35 (1)	0.00 (0)	1.72 (15)
Lymphosarcoma and reticulosarcoma	3.33 (1)	0.00 (0)	2.24 (3)
Hodgkin's disease	0.00 (0)	0.00 (0)	7.19 (4)**
Other lymphatic and haematopoietic CA	0.00 (0)	0.00 (0)	1.18 (8)
Other/unspecified CA	0.00 (0)	1.21 (2)	1.76 (19)*
Non-malignant respiratory disease	1.32 (4)	1.48 (11)	1.42 (85)**
Emphysema	2.39 (1)	2.21 (4)	1.89 (16)*
Pneumoconioses and other respiratory diseases	3.73 (2)	2.24 (4)	1.61 (46)**
Chronic renal disease	3.95 (3)	1.23 (1)	0.92 (4)

*95% confidence interval excludes the null value (1.0).
**99% confidence interval excludes the null value (1.0).

the cohort was restricted to men without known employment in other aspects of the uranium industry.

DISCUSSION

Uranium exposure presents both chemical and radiological hazard potentials. Both the chemical and radiological toxicity are influenced by the biological solubility of a given uranium compound. Poorly soluble uranium compounds are cleared slowly from the lungs and pose a potential internal radiation hazard. More soluble compounds are absorbed rapidly from the lungs, decreasing the radiation hazard, but increasing the potential for renal toxicity.[19 20] In the ore handling and preparation areas of the mills, the uranium in ore dusts consists mostly of insoluble uranium oxides with a relatively small fraction of the more soluble uranium compounds. The potential for exposure to the long lived alpha emitters (uranium-238, uranium-234, thorium-230, radium-226, and lead-210) is greatest in these areas of the mill. In the yellowcake drying and packaging areas of the mill, the uranium in yellowcake consists of a complex mixture of uranium compounds of varying solubility. The composition and solubility of the yellowcake product depends on the drying temperature employed.[19 21] In mills that dry the product at relatively low temperatures (100–150°C), the yellowcake product is high in ammonium diuranate [$(NH_4)_2U_2O_7$] which is highly soluble in lung fluids; in mills that dry the product at relatively high temperatures (370–538°C), the yellowcake is high in uranium oxide (U_3O_8) which is mostly insoluble in lung fluids.[21 22] Based on available data on drying temperatures and drying equipment, four of the five conventional mills in this study used relatively high drying temperatures. The fifth mill did not prepare a dried yellowcake product; rather, it produced filter press cake or a uranium product liquor, depending on the year of operation. Accordingly, most mill workers in this study worked in mills that probably produced yellowcake of relatively low solubility.

Both human and animal data suggest that insoluble uranium compounds and thorium accumulate in the tracheobronchial lymph nodes.[23–26] Because of this, it has been suggested that studies of early uranium workers evaluate the effects on lymphatic tissues.[25] In the previous study of workers at the mills in this study, a significant increase in mortality from lymphatic and haematopoietic malignancies other than leukaemia was observed after 20 years latency, based on six deaths.[7] We also found an excess in mortality from lymphatic and haematopoietic malignancies other than leukaemia but the magnitude of the excess was less than the excess observed in the previous study. The observed excess was due to an excess in both Hodgkin's disease mortality and lymphosarcoma and reticulosarcoma mortality based on four observed deaths each. The ability to evaluate exposure response relations, using duration of employment as a surrogate of exposure, was limited by the small number of observed deaths from these cancers. Of the eight observed deaths due to Hodgkin's disease, lymphosarcoma, and reticulosarcoma in this study, three were observed in the previous study and one was observed in the study by Archer and colleagues.[8]

Hodgkin's disease and non-Hodgkin's lymphoma, a group of lymphomas which includes lymphosarcoma and reticulosarcoma, have not been clearly linked to radiation.[27 28] Data on the risk of death from Hodgkin's disease and non-Hodgkin's lymphoma among uranium or thorium workers are limited. An increased risk of Hodgkin's disease mortality and lymphosarcoma and reticulosarcoma mortality has been observed among uranium processing workers at the Fernald Feed Materials Production Center near Cincinnati, Ohio (SMR = 2.04, 95% CI 0.74 to 4.43, obs = 6; and SMR = 1.67, 95% CI 0.72 to 3.29, obs = 8, respectively)[29] and thorium processing workers (SMR = 1.64, 95% CI 0.33 to 4.79, obs = 3; and SMR = 1.14, 95% CI 0.23 to 3.34, obs = 3, respectively),[30] but not among uranium processing workers at the Y-12 plant at Oak Ridge, Tennessee[31] and Mallinckrodt Chemical Works in St Louis, Missouri[32] or among a combined cohort of uranium and other miners from 11 studies.[33] Hodgkin's disease mortality and incidence and non-Hodgkin's lymphoma incidence was associated with cumulative external radiation dose among workers at the Springsfield uranium production facility; the effects of internal exposures were not evaluated.[34] In general, these studies, like the current study, are limited by the small number of deaths from Hodgkin's disease and non-Hodgkin's lymphoma among exposed workers.

A new finding in this update not previously reported was a small increase in mortality from cancer of the trachea, bronchus, and lung, particularly relative to state rates. We also observed an increased risk of mortality from non-malignant respiratory disease. Mortality from lung cancer was higher based on state rates than US rates, whereas mortality from non-malignant respiratory disease was lower based on state rates than US rates. This is consistent with the relatively low smoking attributable mortality and relatively high chronic obstructive lung disease mortality in Arizona, Colorado, and New Mexico compared to other states.[15] The reason for the discrepancy in smoking-attributable mortality

and chronic obstructive lung disease mortality in many inland western states is unknown. However, the results suggest that regional differences in mortality may explain, in part, the observed excess in non-malignant respiratory disease mortality based on US rates.

The excess in both lung cancer mortality and emphysema mortality was greater among workers hired prior to 1955, when there was little emphasis on dust control and exposures to uranium and silica containing dusts were presumably higher. However, mortality from lung cancer and non-malignant respiratory disease was inversely related to duration of employment. We found no evidence that workers who were hired prior to 1955 were more likely to be short term workers. The inverse relation between lung cancer and emphysema mortality and duration of employment in this study may be a reflection of the healthy worker survivor effect, in which individuals who remain in the workforce over time tend to be healthier than those who leave.[36] Duration of employment may also be a poor surrogate of exposure in this study since exposures are thought to have varied considerably by mill area and over time.

Some data suggest that uranium workers other than miners may be at increased risk of lung cancer[29 31] and non-malignant respiratory disease.[37] Uranium ore dust has been shown to induce pulmonary lesions in animals[23 38 39] and lung cancer in rats.[40] Silica exposure has been reported to lead to the development of silicosis, emphysema, obstructive airways disease, and lymph node fibrosis.[41] Although the carcinogenicity of silica continues to be debated in the scientific community, several investigators have showed an increased risk of lung cancer among workers exposed to silica.[42–44] Vanadium containing compounds have known acute respiratory effects,[45] but it is less clear whether exposure to vanadium can lead to chronic non-malignant respiratory disease.[45 46] In this study, we only observed three deaths from silicosis and unspecified pneumoconioses. The majority of the excess in non-malignant respiratory disease mortality was due to mortality from emphysema and other respiratory disease.

Other potential explanations also exist for the observed excesses in mortality from lung cancer and non-malignant respiratory disease mortality. Smoking data are not available for this cohort, and differences in smoking habits between the cohort and the general population may partially explain the excesses observed. White men in the Colorado Plateau uranium miners cohort were heavy smokers,[6 47] but it is unknown whether the smoking habits of uranium mill workers who never worked underground in uranium mines would be similar to these miners. Even if the mill workers in this study were more likely to smoke than the general population, other investigators have shown that smoking is unlikely to account for SMRs above 1.3 for lung cancer and other smoking related diseases.[48] Other potential factors that may contribute to these excesses include unknown employment in underground uranium mines and employment in other mines with increased levels of radon and radon decay products. It is unlikely that the cohort included many mill workers who also worked as uranium miners. Mill workers who also worked in uranium mines were identified by reviewing the work history records and by matching the cohort to a NIOSH file of over 18 000 uranium miners. All identified uranium miners were excluded from the final cohort. However, members of the cohort may have been more likely to work in other types of mines than the general population.

We found a small non-significant excess in chronic renal disease when using US rates as a comparison; this excess was not apparent when only deaths between 1960 and 1998 were analysed (both underlying cause and multiple cause). Renal effects have been observed among silica exposed workers. Goldminers and industrial sand workers exposed to silica have been found to be at excess risk of death from renal disease and to have increased renal disease incidence.[16 49 50] Low level β_2 microglobulinuria and aminoaciduria has been observed among uranium mill workers exposed to soluble uranium compounds at a mill not in the current study,[9] but little data on chronic renal disease mortality among uranium workers exist. An increase in mortality from chronic nephritis (SMR = 1.88; 95% CI 0.75 to 3.81) was observed among uranium processing workers at Mallinckrodt, based on six observed deaths.[32] An excess in chronic renal disease mortality has been observed among uranium miners (SMR = 1.6; 95% CI 0.7 to 3.0, obs = 9), but the observed excess was not related to duration of employment.[6]

This study may have underestimated the risk of ESRD and renal disease mortality associated with uranium milling. We observed an excess in chronic renal disease mortality during the follow up period 1940–59, but not during the follow up period 1960–98. This suggests that the exclusion of cohort members who died or were lost to follow up prior to 1960 may have been a significant limitation in our ability to evaluate the risk of ESRD and chronic renal disease mortality using multiple cause of death data. Because the cohort is relatively old, approximately 22% of the cohort was excluded from the analysis of ESRD because they died or were lost to follow up before the ESRD PMMIS is first considered complete, which also reduced the statistical power of the ESRD analysis. In addition, the majority of the mill workers in this study were probably exposed to relatively insoluble forms of uranium. The risk of renal disease may be higher in mills using relatively low drying temperatures where the potential for exposure to soluble forms of uranium is greater. The study evaluated chronic renal disease mortality and ESRD and was not able to evaluate the risk of less severe renal effects.

In conclusion, we observed an excess in mortality from haematopoietic and lymphatic malignancies other than leukaemia, trachea, bronchus, and lung cancer, non-malignant respiratory disease, and chronic renal disease. Some of these excesses were based on a small number of deaths and the confidence intervals around the point estimates were wide. Limitations include the lack of smoking data, small cohort size and limited power to detect a moderately increased risk of some of the a priori outcomes of interest, and the inability to evaluate exposure-response relations using individual estimates of exposure to uranium, silica, and vanadium. Because of these limitations and the lack of a positive trend between the observed excesses and duration of employment, firm conclusions about the relation of the observed excesses and mill exposures are not possible.

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Appendix 5

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Cancer mortality in a Texas county with prior uranium mining and milling activities, 1950–2001

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Abstract

Uranium was discovered in Karnes County, Texas, in 1954 and the first uranium mill began operating in 1961 near Falls City. Uranium milling and surface and *in situ* mining continued in Karnes County until the early 1990s. Remediation of uranium tailings ponds was completed in the 1990s. There were three mills and over 40 mines operating in Karnes County over these years and potential exposure to the population was from possible environmental releases into the air and ground water. From time to time concerns have been raised in Karnes County about potential increased cancer risk from these uranium mining and milling activities. To evaluate the possibility of increased cancer deaths associated with these uranium operations, a mortality survey was conducted. The numbers and rates of cancer deaths were determined for Karnes County and for comparison for four 'control' counties in the same region with similar age, race, urbanisation and socioeconomic distributions reported in the 1990 US Census. Comparisons were also made with US and Texas general population rates. Following similar methods to those used by the National Cancer Institute, standardised mortality ratios (SMRs) were computed as the ratio of observed numbers of cancers in the study and control counties compared to the expected number derived from general population rates for the United States. Relative risks (RRs) were computed as the ratios of the SMRs for the study and the control counties. Overall, 1223 cancer deaths occurred in the population residing in Karnes County from 1950 to 2001 compared with 1392 expected based on general population rates for the US. There were 3857 cancer deaths in the four control counties during the same 52 year period compared with 4389 expected. There was no difference between the total cancer mortality rates in

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Karnes County and those in the control counties (RR = 1.0; 95% confidence interval 0.9–1.1). There were no significant increases in Karnes County for any cancer when comparisons were made with either the US population, the State of Texas or the control counties. In particular, deaths due to cancers of the lung, bone, liver and kidney were not more frequent in Karnes County than in the control counties. These are the cancers of *a priori* interest given that uranium might be expected to concentrate more in these tissues than in others. Further, any radium intake would deposit primarily in the bone and radon progeny primarily in the lung. Deaths from all cancers combined also were not increased in Karnes County and the RRs of cancer mortality in Karnes County *before* and in the early years of operations (1950–64), shortly after the uranium activities began (1965–79) and in two later time periods (1980–89, 1990–2001) were similar, 1.0, 0.9, 1.1 and 1.0, respectively. No unusual patterns of cancer mortality could be seen in Karnes County over a period of 50 years, suggesting that the uranium mining and milling operations had not increased cancer rates among residents.

1. Introduction

In Karnes County, Texas, concern has been expressed that cancer rates might be greater than expected due to uranium mining and milling activities that began in the 1950s (Brender 1987, 1989). The concerns were related to potential environmental releases into the air and ground water from operating the three mills and over 40 uranium mines, including the transport of uranium ore. The activities associated with uranium extraction from ore would produce solid and liquid wastes. The wastes, called tailings, contain most of the radionuclides present in the ore, including thorium, radium and other decay products. Radon and radon progeny are a secondary source of possible exposure in mines, mills and tailings ponds. The tailings ponds, surface mines, runoff collection ponds, ore transport and the mills (extraction facilities) are the potential exposure pathways to humans (NCRP 1993).

A small cytogenetic study in Karnes County (Au *et al* 1995) and a recent exploratory geographical correlation study in Spain (López-Abente *et al* 2001) have suggested that uranium operations might increase cancer risk, but both investigations had methodologic deficiencies that limited interpretation. Studies of cancer mortality (1979–88) and cancer incidence (1976–80) conducted previously by the Texas Department of Health, provided no indication of unusually high cancer rates in populations living in Karnes County (Brender 1987, 1989) but it is possible that the time between potential exposure and occurrence of disease may have been too short to demonstrate an effect. To provide additional information over a longer time period than previously possible, we conducted a county mortality study contrasting cancer rates in Karnes County before, during and after the uranium operations began. The current investigation includes more calendar years than previously possible, over 50 years, and incorporates a comparison with nearby counties with similar demographic characteristics. The investigative methods followed are similar to those used by the National Cancer Institute in a study of nuclear installations throughout the United States (Jablon *et al* 1990, 1991).

2. Methods

2.1. Uranium mining, transportation, milling and waste disposal activities

Karnes County is south of San Antonio, Texas, in the central coastal plain area in the southern part of the state. The uranium mining activities around Karnes County began in 1959 and the

first uranium mill began operating in 1961. The uranium ore was transported from surface mines to mills where the uranium concentrate U_3O_8 (yellowcake) was produced. There were three conventional uranium mills and over 40 *in situ* and surface mines operating in Karnes County for several decades. *In situ* or solution mining is a method where a leaching solution is injected through wells into the ore body to dissolve the uranium. Production wells are then pumped to bring the uranium-bearing solution to the surface for eventual extractions. There were no underground mines. After the uranium ore was processed, the waste material, called tailings, was placed in tailings piles or ponds. The tailings contain unrecovered uranium and amounts of other radionuclides including thorium and radium (Ruttenber *et al* 1984, Eisenbud 1987, Ibrahim *et al* 1990, Veska and Eaton 1991, Thomas 2000). Radon gas released from the decay of radium would be dispersed and diluted into the atmosphere. Remediation of the Falls City mill site was completed in 1994 (DoE 2002). The Conquista mill was decommissioned in the early 1980s and the tailings pond was capped and closed by the early 1990s. The Panna Maria mill was decommissioned in the early 1990s and the tailings pond was capped and closed in the late 1990s.

Because the uranium mining and milling processes in Karnes County did not involve any uranium enrichment, workers and the public were not exposed to enriched radioactive materials or wastes. Natural uranium ores are not generally considered to present an external radiation hazard (NCRP 1993, Priest 2001). Exposure to airborne ore dust is a principal source of potential exposure. The Texas Department of Health began monitoring the environment around uranium mines and recovery facilities in 1961 and in 1988–89 instituted a sampling programme in response to public concerns about possible exposure to radioactive materials from the uranium recovery activities (Meyer 1990). The sampling programme included private water supplies, radon in homes, radon in schools and radioactivity in milk and meat. There was no evidence for increased levels of radioactive materials in Karnes County compared with other parts of Texas; if anything, the average radon concentrations in homes (0.8 pCi l^{-1}) was lower than in other parts of the state. The concentration of uranium in milk samples was also below the minimum detectable level of the measurement equipment.

2.2. *Cancers considered in the study*

After ingestion or inhalation, uranium distributes within the body to tissues depending on its chemical properties and route of intake (ICRP 1995a, 1995b). Inhalation of uranium would result in deposition within the lung and pulmonary lymph nodes. The bone, kidney and liver are the other most probable sites of deposition and exposure, albeit at a lower level than for the lung. In general, the solubility of natural uranium is very high (ICRP 1995a, 1995b, Priest 2001) which implies a relatively short residence time within the body before being eliminated by normal processes. The kidney is also an organ of interest because of possible damage related to the chemical properties of uranium, a heavy metal.

The following kinds of cancer were studied on the basis of the likely deposition of uranium in body tissue mentioned above: cancers of the lung, bone, liver and kidney. In addition, it is known that substantial ingestion of radium has increased the risk of bone cancer among dial painters (Fry 1998) and extensive exposure to radon and its progeny has increased the risk of lung cancer among underground miners (Lubin *et al* 1995, NRC 1999). On the basis of the knowledge of cancers found increased after high dose and high dose rate external exposures to gamma or x-rays, cancers of the stomach, colon, female breast and thyroid gland and leukemia were studied (Boice *et al* 1996, UNSCEAR 2000). For completeness, other cancers were included, including those not frequently found to be increased in exposed populations, such as cancers of the oesophagus, pancreas, cervix uteri and corpus uteri and prostate, malignant melanoma of the skin, Hodgkin's disease, non-Hodgkin's lymphoma and multiple myeloma.

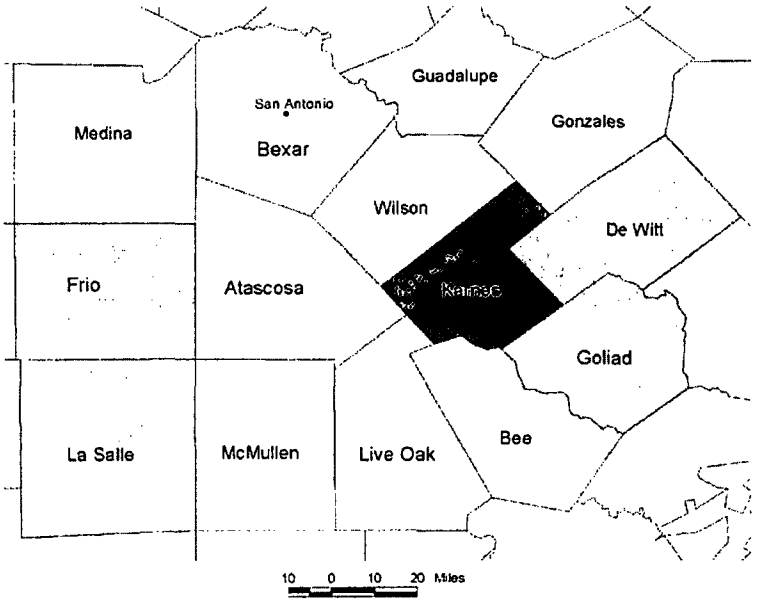

Figure 1. A map of South Texas containing Karnes County and the four control counties (Frio, La Salle, DeWitt and Goliad). The dots in Karnes County represent the prior location of 43 mines and 3 mills (Railroad Commission of Texas, Surface Mining and Reclamation Division map).

2.3. Mortality data

Counties are the smallest areas for which both population estimates and annual counts of the number of deaths for specific causes are readily available back to 1950 from the National Center for Health Statistics and the US Census Bureau (NCI 1999). Cancer mortality data for Texas at the county level were available from the National Cancer Institute from 1950 to 1995 (NCI 1999) and from the Texas Department of Health from 1996 to 2001 (TDH 2002).

2.4. Study county (figure 1)

Karnes County constituted the study county where the residing population had the potential for exposure to uranium ore and its decay products from the surface and *in situ* mining and milling activities, including transportation and any possible exposures from tailings ponds.

2.5. Control counties

Four comparison counties were selected (table 1). Control counties were matched to Karnes County by the following characteristics: percentages of persons in the population that were white, Hispanic, urban, rural, employed in manufacturing, below the poverty level, over age 64, and high school graduates, and mean family income and population size. Data were obtained from the 1990 census (USDC 1992). Data on diet, smoking and other potential cancer risk factors are not readily available at the county level, but choosing control counties from the same region as the study counties, i.e., South Central Texas, helps minimise differences in these and other factors.

Table 1. Selected characteristics of residents in Karnes County and in four control counties in South Central Texas.

County	Total population 1990	Percentages (%)									Median household income ($10 000)
		Male	White	Black	Hispanic	Rural	>64 y	Below poverty	High school graduate	Employed	
Study county											
Karnes	12 455	48	97	3	47	46	16	36	51	50	16.2
Control counties											
DeWitt	18 840	47	89	11	24	53	19	25	55	49	18.0
Frio	13 472	49	98	1	72	29	10	38	50	53	14.1
Goliad	5 980	48	93	7	36	100	16	18	63	53	21.4
La Salle	5 254	50	99	0	75	29	14	37	45	51	15.6
All control											
	43 546	48	93	6	47	49	15	29	56	51	18.5

2.6. Statistical analyses

Counts of deaths by cause, sex, race and five year age group were obtained for each of the five selected counties for each year from 1950 to 2001. Estimated annual county populations by sex, race and age group were obtained by interpolation in census counts for 1950–69 and for later years decennial censuses prepared by the Bureau of the Census (NCI 1999, Jablon *et al* 1990). Population data for counties in Texas were also available from the Texas Department of Health (TDH 2002). For each type of cancer and each county the 'expected' number of deaths, based on concurrent US experience, was calculated for the 52 year study period (NCI 1999, Marsh *et al* 1998). The expected numbers were obtained by multiplying annual US cancer death rates by the estimated populations, stratified by five year age group and sex. Counts were then summed for Karnes County and for all four of the corresponding control counties. Counts of observed and expected deaths were then summed over the following time periods: 1950–64 (before and just after the uranium operations began), 1965–79, 1980–89 and 1990–2001, thus producing numbers of deaths observed and expected generally *before, during* and *after* uranium activities began. This approach is the same as what was done previously in the United States by the National Cancer Institute (NCI) using similar databases and statistical programs (Jablon *et al* 1990, NCI 1999). Comparisons with Texas cancer death rates were also made but are not presented because computed RRs, described below, did not differ appreciably from those based on US general population rates.

The ratio of the actual number of deaths observed to the number expected at US rates is the standardised mortality ratio (SMR). Ratios of the SMRs for the study and control counties were called RRs. The difference between each RR and 1.00 was assessed by calculation of the probability that a difference of the observed magnitude, or larger, might have arisen by chance (Breslow and Day 1987, Jablon *et al* 1990, Mantel and Ederer 1985). A 95% confidence interval that contains 1.00 indicates that chance is a likely explanation for any observed differences in cancer mortality rates between Karnes County and the control counties.

Strata containing three or fewer cancer deaths are not presented but are listed as LT4 to denote 'less than four'. This is to abide by the confidentiality requirements for using the NCI and National Center for Health Statistics database. The concern is the possibility that individuals with certain characteristics might be identified if the number of deaths were small.

Table 2. The number of cancer deaths occurring in Karnes County and in the four control counties in South Central Texas, 1950–2001. 'LT4' denotes 'less than 4'.

	Number of deaths	
Cancer (ICD-9)	Karnes County	Control counties
Oesophagus (150)	20	58
Stomach (151)	72	207
Colon/rectum (153, 154)	168	456
Pancreas (157)	69	217
Lung (162)	224	653
Melanoma/skin (172)	21	58
Female breast (174)	79	246
Cervix uteri (180)	18	72
Corpus uteri (182)	5	27
Ovary (183)	28	97
Prostate (185)	76	257
Urinary bladder (188)	17	87
Kidney/renal pelvis (189)	19	105
Liver (155)	27	109
Bone (170)	11	23
Connective tissue (171)	LT4	15
Brain and CNS (191, 192)	24	78
Thyroid (193)	LT4	20
Non-Hodgkin's lymphoma (200, 202)	38	121
Hodgkin's disease (201)	12	22
Multiple myeloma (203)	22	52
Leukemia (204–8)	59	161
All cancers (140–208)	1223	3857

3. Results

In 1990, the total number of residents within Karnes County and the four control counties were 12 455 and 43 546, respectively. During the 52 years of study, 1950–2001, nearly 650 000 person-years of observation were accrued by people living in Karnes County and just over 2260 000 person-years among people living in the control counties. The control counties were similar to the study counties with regard to demographic indicators of cancer risk such as age, race and various measures of socioeconomic status (table 1). Over 90% of the population studied were listed on the census as white, including 47% Hispanic, just over 15% were older than 64 years and over 51% had graduated from high school. The median household income in 1990, about $16 200 per year, for the study population was somewhat lower than that for the control population. Both study and control counties were about 50% rural.

Table 2 shows the number of cancer deaths occurring in Karnes County and the control counties over the years 1950–2001. There were 1223 cancer deaths within Karnes County (1392 expected; SMR = 0.88) and 3857 cancer deaths within the four control counties (4389 expected; SMR = 0.88). The RR for total cancer mortality in Karnes County compared to the control counties was 1.00 (95% CI 0.9–1.1). The most frequent cancer deaths were of the lung, colon and rectum, female breast, prostate and stomach. There were 224 lung cancer deaths, 11 bone cancer deaths, 19 kidney cancer deaths, 27 liver cancer deaths, 59 leukemia deaths and 79 deaths due to female breast cancer in Karnes County.

Table 3 shows the SMRs for all types of cancer combined for the time periods 1950–64, 1965–79, 1980–89 and 1990–2001. The SMRs comparing study and control counties

Table 3. Mortality due to all types of cancer, all ages and sexes combined over four time periods, 1950–2001, in Karnes County and in the four control counties. ('Obs' stands for 'Observed'.)

	Calendar years of death									
	1950–64		1965–79		1980–89		1990–2001		All	
	Obs	SMR[a]	Obs	SMR[a]	Obs	SMR[a]	Obs	SMR[a]	Obs	SMR[a]
Karnes County	267	0.9[c]	331	0.9[c]	279	0.9	346	0.9[c]	1223	0.88[c]
Control counties	799	0.8[c]	1102	0.9[c]	818	0.8[c]	1138	0.9[c]	3857	0.88[c]
RR[b]	1.0		0.9		1.1		1.0		1.0	

[a] SMR is the observed number of cancers divided by that expected based on rates within the general population of the United States.
[b] Estimated RR taken as the ratio of the SMR in Karnes County with that in the four control counties.
[c] $p < 0.05$.

with the general population of the United States were slightly below 1.00 for each of the four time periods. The RRs contrasting total cancer mortality in Karnes County with that in control counties before and after uranium operations began were similar and varied between 0.9 and 1.1.

Table 4 concerns specific causes of death for both children and adults and shows very little difference in cancer mortality rate between study and control counties over the four time periods. There were three statistically significant RRs. Colon and rectal cancer was increased significantly overall (RR 1.17) which was due to a significant elevation (RR 1.6) in 1950–64 and prior to the major onset of uranium operations. Cancer of the kidney was significantly low (RR 0.58). Lung cancer (RR 1.08), leukemia (RR 1.15), bone cancer (RR 1.35), female breast cancer (RR 1.01), liver cancer (RR 0.81) and non-Hodgkin's lymphoma (RR 1.04) occurrences were close to expectation and were not statistically distinguishable from no risk (RR 1.0). Of the 23 RRs presented in table 4 for 1950–2001, nine were slightly above 1.0, ten were slightly below 1.0 and four were essentially equal to 1.0—a distribution consistent with the random variations commonly seen in population statistics. There was no suggested pattern for increasing risks over time for any specific cancer.

For childhood cancer mortality, including leukemia, the RR comparing Karnes County with the control counties was 1.2 ($n = 7$) before most uranium operations began (1950–64) and 1.3 ($n = 8$) after the onset of the mining and milling activities (1965–2001) (data not shown). Overall in Karnes County, there were 6 deaths due to leukemia in children versus 5.1 expected based on general population rates. Based on a total of 59 leukemia deaths, there were no significant elevations in any time interval or overall (RR 1.15; 95% CI 0.9–1.1). Only 2 deaths from thyroid cancer were observed versus 2.7 expected.

4. Discussion

Compared to similar counties in South Central Texas, no increase in cancer mortality was found in Karnes County where there was potential for radiation exposures from uranium mining and milling activities, including potential exposures from transportation of ore and from tailings ponds. No significant excess deaths were found for cancers of the lung, bone, liver or kidney, or non-Hodgkin's lymphoma, i.e., in those tissues where deposition of uranium might have been anticipated had there been intake (ICRP 1995a, 1995b). Any intake of radium would have lodged primarily in bone and radon decay products would have deposited primarily in lung.

Table 4. RR of mortality due to selected cancers in Karnes County versus the four control counties for four time periods during 1950–2001. ('Obs' denotes the observed cancer deaths within Karnes County, 'LT4' denotes that the observed number of deaths is less than 4 and 'RR' denotes the estimated relative risk taken as the ratio of the SMR in Karnes County to that in the four control counties.)

	Calendar year of death											
	1950–64		1965–79		1980–89		1990–2001		Total 1950–2001			
Cancer (ICD-9)	Obs	RR	Obs	RR	Obs	RR	Obs	RR	Obs	RR	95% CI	
Oesophagus (150)	5	1.4	4	0.7	LT4	1.1	9	1.1	20	1.06	(0.6–1.8)	
Stomach (151)	29	1.3	19	1.0	11	0.9	13	1.0	72	1.08	(0.8–1.4)	
Colon/rectum (153, 154)	45	1.6[a]	40	0.9	35	1.1	48	1.2	168	1.17[a]	(1.0–1.4)	
Pancreas (157)	14	1.0	22	1.1	20	1.3	13	0.7	69	1.01	(0.8–1.3)	
Lung (162)	0	0.0	59	1.0	73	1.2	92	1.0	224	1.08	(0.9–1.3)	
Melanoma/skin (172)	5	2.0	9	1.7	LT4	0.8	4	0.7	21	1.23	(0.7–2.0)	
Female breast (174)	21	1.3	21	0.9	14	0.9	23	1.0	79	1.01	(0.8–1.3)	
Cervix uteri (180)	9	1.1	4	0.5	LT4	0.8	LT4	0.6	18	0.76	(0.5–1.3)	
Corpus uteri (182)	0	0.0	0	0.0	4	1.8	LT4	0.3	5	0.72	(0.3-1.9)	
Ovary (183)	LT4	0.3	13	1.7	4	0.7	8	1.0	28	0.90	(0.6–1.4)	
Prostate (185)	15	0.9	15	0.7	16	1.0	30	1.2	76	0.95	(0.7–1.2)	
Urinary bladder (188)	5	0.7	4	0.5	4	1.1	4	0.6	17	0.64	(0.4–1.1)	
Kidney/renal pelvis (189)	LT4	0.4	6	0.6	5	0.9	5	0.5	19	0.58[a]	(0.4–1.0)	
Liver (155)	0	0.0	11	1.0	6	0.8	10	0.7	27	0.81	(0.5–1.2)	
Bone (170)	5	2.2	LT4	0.3	LT4	—	LT4	0.9	11	1.35	(0.7–2.8)	
Connective tissue (171)	LT4	0.7	0	0.0	0	0.0	LT4	1.2	LT4	0.44	(0.1–1.5)	
Brain and CNS (191, 192)	5	0.8	5	0.6	8	1.8	6	0.9	24	0.92	(0.6–1.4)	
Thyroid (193)	0	0.0	LT4	0.4	0	0.0	LT4	0.8	LT4	0.31	(0.1–1.3)	
Non-Hodgkin's lymphoma (200, 202)	LT4	0.7	13	0.9	8	1.2	14	1.1	38	1.00	(0.7–1.4)	
Hodgkin's disease (201)	4	1.8	5	1.5	LT4	—	0	0.0	12	1.79	(0.9–3.6)	
Multiple myeloma (203)	LT4	0.7	4	1.0	6	1.1	11	2.0	22	1.37	(0.8–2.3)	
Leukemia (204–208)	9	0.7	20	1.3	17	1.7	13	1.0	59	1.15	(0.9–1.6)	
All cancers (140–208)	267	1.0	331	0.9	279	1.1	346	1.0	1223	1.00	(0.9–1.1)	

[a] $p < 0.05$.

Knowledge about radiation carcinogenesis has accumulated during the past 50 years and is helpful in interpreting the study findings (UNSCEAR 1994, 2000, IARC 2000, 2001). Although radiation-induced leukemia may occur as soon as two years after exposure, other cancers such as those of the lung and breast develop more slowly and are unlikely to be identified in mortality data for ten years or more after radiation exposures. Because mortality data were available for over 40 years after the uranium mining activities began in 1959, residents of the surrounding area could be evaluated for a long enough period of time to accumulate sufficient exposure to detect any increase in mortality due to cancer if one were present. Comparing Karnes County with the four nearby control counties, the RR for all cancer mortality ranged from 0.9 to 1.1 over the 52 years of study. The fact that significant differences were not found in our survey for the periods *before, during* or *after* the uranium mining and milling activities

began provides evidence that the mining and milling operations have not adversely affected the occurrence of cancer among County residents. Our survey is thus consistent with other studies of persons living near uranium processing facilities in the US (Jablon *et al* 1990, Boice *et al* 2003a, 2003b), and also with studies of workers heavily exposed to uranium during processing activities (CRS 2001) where no increased cancer risks were observed.

Because many workers involved in uranium mining and milling activities lived in Karnes County, their inclusion within the study population probably enhances our power to detect a radiation association given that worker exposures would be expected to be much greater than residential exposures. Studies of over 120 000 workers at uranium milling, fabrication and processing facilities, however, have not found any consistent links between uranium exposures and increases in any cancer or leukemia (McGeoghegan and Binks 2000a, 2000b, CRS 2001, IOM 2001, IARC 2001). Specifically, no increases in cancers of the lung, liver or bone or lymphoma were observed among these uranium workers, i.e., in those tissues where the probable distribution of uranium was highest (ICRP 1995a, 1995b, IARC 2001). Uranium, similar to radium or plutonium, would deposit primarily in bone and not bone marrow, minimising the likelihood of a leukemogenic exposure to the uncommitted stem cells that reside more centrally in the marrow (Priest 1989, 2001). Thus the absence of a leukemia risk is not surprising. A recent geographical correlation study in Finland also found no evidence for increased leukemia rates among communities with high levels of uranium in their water supplies (Auvinen *et al* 2002). Radon and its decay products have caused lung cancer among underground miners (Lubin *et al* 1995, NRC 1999) but no other cancer or leukemia has been found elevated among the over 64 000 heavily exposed miners studied (Darby *et al* 1995). Substantial intake of radium has caused excess bone cancers among dial painters, but no risk was seen at low to moderately high doses (<10 Gy skeletal dose) and no other cancers were associated with radium intake except a rare carcinoma of the sinuses attributable to the build-up of radon from the radium decay (Rowland *et al* 1978, Polednak *et al* 1978, Fry 1998, Priest 2001).

Reports of small clusters of childhood leukemia around nuclear installations in the United Kingdom in the 1980s prompted several large scale systematic surveys around the world (UNSCEAR 1994). Subsequent surveys in other counties failed to confirm a link between childhood leukemia or any other cancer and proximity to nuclear installations (Doll *et al* 1994, Doll 1999). Several geographical correlation studies around nuclear installations in Spain have been published recently suggesting an increase in cancer mortality in areas containing uranium processing facilities, including one that also contained a nuclear waste storage facility, but not in areas with nuclear power plants (López-Abente *et al* 1999, 2001). However, the cancer mortality rates in the towns near the uranium operations were below expectation based on general population rates (SMR 0.88) and it was the even lower rates among the more distant towns (50–100 km) used as control that produced the apparent elevation. The areas with uranium facilities, then, did not experience elevated cancer rates but rather the control areas experienced unusually low cancer rates. This suggests that the residents of the control areas may not have been similar to the residents of towns near uranium processing facilities and such non-comparability tempers interpretation (Laurier *et al* 2002). Further, cancer risks overall and for lung cancer and kidney cancer in particular were lower in the towns nearest (<15 km) to the uranium facilities than in the towns located further away (15–30 km), which is just the opposite to what would be expected if radiation were a contributing factor. In addition, the elevated mortality rates were gender specific in that lung cancer increases were seen only in males and not females, whereas kidney cancer increases were seen only in females and not males. Such differences are also not consistent with a possible effect of environmental exposures, because any exposures common to both sexes would be expected to affect both males and

females and not just one or the other. Similarly, a slight increase in leukemia reported in the Spanish study (López-Abente *et al* 1999) is not in accord with what is known about the distribution of uranium in the body after intake, i.e., exposure to the leukemia-producing cells is minuscule (Bender *et al* 1988, Priest 1989). Further a radiation link between leukemia and living near nuclear installations has been discounted after extensive epidemiologic study (UNSCEAR 1994, Laurier *et al* 2002). Finally, uranium processing facilities in the US have not been correlated with increased cancer mortality (Jablon *et al* 1990, Boice *et al* 2003a) or cancer incidence in nearby populations (Boice *et al* 2003b). Thus the exploratory correlation studies in Spain must be interpreted with caution, since the mortality excesses and deficits may be attributable to bias if control area residents were not comparable to study area residents in terms of cancer risk factors or, as mentioned by the authors, to chance when so many hundreds of comparisons are made (11 different cancers, 8 installations and 3 distances).

A cross-sectional cytogenetic analysis has also been conducted among a small number of Karnes County residents to investigate whether living near uranium mining and milling activities might be associated with chromosome aberrations in circulating lymphocytes and also with abnormal DNA repair processes (Au *et al* 1995). Bloods were analysed for 24 persons, primarily women, potentially exposed to uranium and other radionuclides and for 24 persons presumably non-exposed. The participation rate was very low, about 30% of those initially selected, and only 6 of the 48 participants were males, indicating the possibility of selection bias. Although the frequency of all types of chromosome aberration combined was slightly increased among those presumably exposed to radiation, the difference was not statistically significant. Further, dicentrics, a type of unstable chromosome aberration found to be increased in populations continuously exposed to environmental radioactivity (Wang *et al* 1990, Upton 1990), was actually higher among the presumed non-exposed and this difference approached statistical significance ($p = 0.06$). Thus there was no evidence that radiation exposure from uranium mining and milling operations resulted in increased levels of chromosome breakage among residents of Karnes County.

An abnormal DNA repair response was also reported among the exposed subjects based on a 'challenge assay' developed by the authors who concluded that prior radiation exposure caused these DNA repair problems (Au *et al* 1995). In addition to the substantial uncertainties associated with small numbers, poor participation rates and the potential for selection bias, the study has other serious deficiencies. First, there was no attempt to estimate radiation exposure to any group, so it is uncertain whether the exposed group actually received more exposure than the non-exposed. Second, the assay, which apparently has not been validated by other laboratories, appears to have been misapplied. The potential exposure is from uranium, an alpha particle emitting radionuclide that deposits energy mainly in the lung and bone. Because alpha particles have little penetrating power, circulating lymphocytes would be expected to demonstrate little if any damage since the stem cells within the bone marrow would not be reached (Bender *et al* 1988, Priest 1989, Lloyd *et al* 2001). Third, the results are not internally consistent. It is not logical that chromosomal aberrations would not be increased in a radiation-exposed group characterised by an abnormal DNA repair processes (somehow associated with this same radiation). For example, in patients with severely defective DNA repair mechanisms, such as ataxia telangiectasia, exposure to radiation results in substantial elevations in chromosome aberrations (IARC 2000). Fourth, cytogenetic studies are substantially limited in their ability to detect any effect from low protracted environmental exposures. In addition, several experimental cellular studies have found that low dose radiation can enhance the repair capabilities of cellular DNA subsequently exposed to higher doses (adaptive response) (UNSCEAR 1994); and not damage them as postulated by (Au *et al* 1995). Finally the authors' claim that their assay results indicate that residents have increased health risks from uranium

exposures (Au *et al* 1998) is speculative and unproven. Chromosome aberrations, including dicentrics, have been reported to be increased in areas of high natural background radiation due to thorium contaminated soil (similar to the postulated exposure conditions associated with the uranium mining and milling activities), yet no health effects have been identified in large populations residing their entire lives in such areas in China (Wang *et al* 1990, Wei *et al* 1997, Boice 2002). Thus radiation-associated damage in circulating lymphocytes is considered a marker of prior exposure but has not been linked to increased health risks (Upton 1990). The Au *et al* (1995) cytogenetics study thus provides no evidence for either increased radiation exposure or adverse health effects among residents of Karnes County.

4.1. Strengths and limitations

This community study covered a long time frame, over 50 years, which enabled detailed analyses of several specific cancers. For Karnes County, comparisons of cancer rates before and after uranium mining and milling activities began could be made. Further comparisons with similar control counties in South Central Texas and with the entire United States were possible. The numbers of total cancer deaths between 1950 and 2001, over 1200, was such that any differences between Karnes County and the control counties could be identified, if they were present. The methodology used was the same as that employed by the National Cancer Institute in a similar, but larger scale investigation of mortality in counties throughout the United States with nuclear facilities: electrical utilities, uranium processing plants and weapons production laboratories (Jablon *et al* 1990, 1991). Like us, the National Cancer Institute concluded that increased cancer risks were not associated with living in counties with nuclear facilities and associated radiation activities.

The cancer data reported herein resulted from routinely collected mortality statistics, but were not from an experimental study where individuals would be randomly assigned exposures and followed forward in time. Information on uranium or other radionuclide exposures, if any, was not known for individuals countywide. Although counties were matched using available data concerning racial composition, urban–rural mix, income and other factors, it is not possible to choose control counties that are exactly comparable with the study county. Counties, for example, can vary with respect to industries, occupations, and lifestyle. Cancer deaths in each county were also compared with the numbers expected on the basis of concurrent US and Texas mortality rates. However, the similarity in cancer rates between Karnes County and the proximal control counties and the Texas and US population for practically all cancers suggest very little incompatibility. The absence of any significant trends in cancer risk over time indirectly addresses the possibility of differences arising solely from inadequate comparison populations.

This study relied mainly on mortality data. Although the accuracy of the cause of death information on death certificates is variable, this inaccuracy is less for cancer than other causes even during the early years of this study (Percy *et al* 1981). Further, the quality of death certificate information would be expected to be similar for Karnes County and the neighbouring counties which comprised the comparison population. Mortality data, however, are not optimal for monitoring such cancers as those of the thyroid or childhood leukemia, for which improved therapy has markedly lowered death rates in recent years while not affecting incidence. The numbers of deaths due to thyroid cancer ($n = 2$) and childhood leukemia ($n = 6$) did not differ from expectation but were too small to be informative in the current study other than to indicate a low mortality risk for these cancers. On the other hand, mortality and incidence rates are highly correlated and mortality nearly equals incidence for many cancers which have high fatality rates, such as cancers of the lung, stomach, bone, connective tissue and liver and

adult leukemia. Further, the mortality data are consistent with the available incidence data from 1976 to 1980 in finding no significant increases for these or any other cancers in Karnes County (Brender 1987). These findings are also consistent with a study of cancer incidence in small geographical areas around two uranium processing facilities in the US which also found no increased cancer rates (Boice *et al* 2003a, 2003b).

Mortality rates have changed over time for a number of reasons including improvements in treatment and changes in lifestyle. For example, mortality rates for childhood leukemia have decreased in the entire United States during the study time period, whereas mortality rates for lung cancer have increased (Jemal *et al* 2003). Our study compares mortality rates in Karnes County with those in nearby control counties by calendar year to account for such changes over time to the extent possible. The increases in lung cancer rates in Karnes County, for example, were similar to the increases seen in the control counties and throughout the nation. The absence of lung cancer deaths in the 1950s reflects both the low death rate during these years and the small numbers at risk of dying.

Data were available only for counties and some residents may have lived at some distance from the uranium mining and milling operations. Local effects might be difficult to detect using county death rates because of any dilution resulting from the inclusion of the populations living far from the uranium mining and milling activities. However, over the years there were over 40 uranium mines, mills and tailings piles and ponds in Karnes County (figure 1) and it also has been suggested that the transport of ore on various county roads might have resulted in some population exposure. Thus, the potential for population exposure was greater than in counties with only one operating facility. Further, the county residents also included workers who probably received higher exposures than were possible from environmental circumstances and their inclusion would probably have increased the chance of finding an effect had there been one.

This was an 'ecological' survey in which the exposures, if any, of individuals are not known. Persons who lived in particular counties at the time of death may not have been long term residents. Some residents will have moved elsewhere and died in another part of the country. Although there have been population changes within Karnes County over the years, e.g., with young people going to college and seeking employment elsewhere or with some workers leaving the area when the mining and milling activities ceased, there has been some relative stability as suggested by the population census. In 1960, for example, the population was 14 995 in contrast to 12 455 in 1990 and 15 446 in 2000 (Website, US Census Bureau).

Despite the limitations inherent in an ecological study of cancer mortality in the counties with and without uranium operations, the methods used have been applied effectively in the past to identify environmental carcinogens when exposures were high and long term. For example, on the basis of findings from the 'cancer maps' constructed from county mortality statistics by the National Cancer Institute (Devesa *et al* 1999a, 1999b), counties with shipyard industries were found to have elevated lung cancer death rates, particularly among men. Subsequent case-control studies in the high risk areas linked the excess lung cancer deaths to occupational exposures to asbestos (Blot *et al* 1978). It might be noted that the NCI cancer maps, similar to our community study, do not indicate that cancer mortality in Karnes County is higher than in the rest of the US or that changes in cancer rates over time differ from those of the rest of the US (Devesa *et al* 1999b).

5. Conclusions

The cancers that might possibly be increased following high exposures to uranium and its decay products, i.e., cancers of the lung, bone, kidney and liver, were not elevated, nor was leukemia, a sensitive indicator of excessive exposure to external gamma radiation. This survey

then provides no evidence that the mining and milling activities increased the rate of any cancer in Karnes County. The ecological nature of the study design, however, tempers the strength of these conclusions.

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Résumé

De l'uranium fut découvert en 1954 dans le comté de Karnes, Texas. Le premier broyeur d'uranium commença à fonctionner en 1961, près de Falls City. Le broyage de l'uranium, son extraction en surface et *in situ* continuèrent, dans ce comté, jusqu'au premières années 90. Dans les années 90, on élimina les dépôts de résidus de broyage. Il existait trois usines de broyage et plus de 40 mines, fonctionnant dans le comté de Karnes, durant ces années; l'irradiation potentielle de la population venait de rejets possibles dans l'environnement, air et eaux souterraines. De temps à autre, il naissait, dans le comté de Karnes, le souci d'une augmentation potentielle du risque de cancers, venant de ces activités d'extraction et de broyage d'uranium. On a établi le relevé de la mortalité pour évaluer la possibilité d'une augmentation des décès par cancer, associée aux opérations sur l'uranium. On a déterminé le nombre et le taux de décès par cancer, pour le comté de Karnes, et on les a comparés aux valeurs pour quatre comtés 'de contrôle' de la même région, présentant des âges, des races, une urbanisation et des distributions socio-économiques semblables, données dans l' US Census de 1990. On fit aussi des comparaisons avec les taux pour la population générale des Etats Unis et du Texas. Par des méthodes semblables à celles employées par l'Institut national du cancer, on a calculé les rapports normalisés de mortalité (SMR); il s'agit du rapport du nombre de cancers dans les comtés, étudié ou de contrôle, au nombre attendu, déduit du taux pour la population globale des Etats Unis. Les risques relatifs (RR) calculés, sont les rapports des SMR pour le comté étudié à celui pour les comtés de contrôle. Au total, il y a eu 1223 décès par cancer dans la population résidant dans le comté de Karnes, entre 1950 et 2001; le nombre attendu en partant de la population générale des Etats Unis était de 1392. Il y eut 3857 décès par cancers dans les quatre comtés de contrôle durant la même période de 52 ans, à comparer aux 4389 attendus. Il n'y a pas de différence entre les taux totaux de mortalité par cancer, dans le comté de Karnes et ceux dans les comtés de contrôle (RR = 1,0; probabilité de 95% pour l'intervalle 0,9–1,1). Quand on a comparé à la population des Etats Unis, à celle du Texas, à celle des comtés de contrôle, on n'a observé aucune augmentation significative dans le comté de Karnes. En particulier, les décès dus à des cancers du poumon, des os, du foie et du rein n'étaient pas plus fréquents dans le comté de Karnes que dans les comtés témoins. Ce sont les cancers à prendre en compte, *à priori*, compte tenu que l'on peut penser que l'uranium se concentre plus dans ces tissus que dans les autres; De plus, toute absorption de radium se déposerait principalement dans les os, et son descendant, le radon, principalement dans les poumons. Les décès venant de l'ensemble de tous les cancers n'avaient pas augmenté dans le comté de Karnes; les RR de mortalité par cancer dans le comté de Karnes *avant* et dans les premières années des opérations (1950–64), peu de temps après que ne commencent les activités sur l'uranium (1965–79) et dans les deux dernières périodes de temps (1980–95, 1990–2001) étaient semblables; 1,0, 0,9, 1,1, 1,0, respectivement. On n'a vu aucun schéma inhabituel de mortalité par cancer dans le

comté de Karnes, sur une période de 50 ans; cela suggère que les opérations d'extraction et de broyage d'uranium n'ont pas augmenté les taux de cancers chez les résidents.

Zusammenfassung

Uran wurde in Karnes County, Texas im Jahre 1954 entdeckt und das erste Uranwerk nahm 1961 in der Nähe von Falls City den Betrieb auf. Uranverarbeitung sowie Tagebau und *in situ* Bergbau wurden in Karnes County bis in die frühen 1990iger fortgesetzt. Die Beseitigung der Uranabfälle in Teichen wurde in den 1990igern abgeschlossen. In diesen Jahren waren drei Werke und mehr als 40 Zechen in Karnes County in Betrieb und die potenzielle Bestrahlung der Bevölkerung wurde durch mögliche Freisetzungen umweltschädlicher Stoffe in die Luft und das Grundwasser verursacht. Von Zeit zu Zeit wurden in Karnes County Bedenken über ein mögliches erhöhtes Krebsrisiko aufgrund dieser Uranabbau- und Verarbeitungsaktivitäten zum Ausdruck gebracht. Zur Bewertung der Möglichkeit einer erhöhten Zahl von Krebstoten aufgrund dieser Uranverarbeitung wurde eine Sterblichkeitsstudie durchgeführt. Die Anzahl der Krebstode wurde für Karnes County ermittelt und im US-Census 1990 verglichen mit vier 'Kontroll'-Counties in derselben Region mit Personen ähnlichen Alters, Rasse, Urbanisierung und soziökonomischen Verteilungen. Weitere Vergleiche wurden angestellt mit allgemeinen Bevölkerungsraten in den USA und Texas. Unter Verwendung ähnlicher Methoden, wie sie vom National Cancer Institute eingesetzt werden, wurden standardisierte Sterblichkeitsverhältnisse (SMRs) berechnet, d.h. die beobachteten Zahlen von Krebsfällen im Studien-und in den Kontroll-Counties wurden mit der Anzahl der zu erwartenden Anzahl verglichen, die aus den allgemeinen Bevölkerungsraten in den USA abgeleitet wurden. Die relativen Risiken (RR) wurden berechnet als Verhältnisse der SMRs für die Studien- und Kontroll-Counties. Insgesamt gab es zwischen 1950 und 2001 1223 Krebstote in der Bevölkerung in Karnes County, verglichen mit 1392, die auf der Grundlage der allgemeinen Bevölkerungsraten in den USA erwartetet worden waren. In den vier Kontroll-Counties gab es im selben Zeitraum über 52 Jahre 3857 Krebstote, verglichen mit 4389 erwarteten. Es gab keinen Unterschied zwischen den gesamten Krebssterblichkeitsraten in Karnes County und denen in den Kontroll-Counties (RR = 1,0; 95% Konfidenzintervall 0,9–1,1). Es gab keine signifikante Zunahme in Karnes County für irgendeine Krebsart, als Vergleiche entweder mit der US-Bevölkerung, dem Staat Texas oder den Kontroll-Counties angestellt wurden. Insbesondere waren Todesfälle aufgrund von Lungen-, Knochen-, Leber- und Nierenkrebs in Karnes County nicht häufiger als in den Kontroll-Counties. Diese Krebsarten sind deshalb von besonderem Interesse, weil sich Uran in diesen Geweben stärker konzentriert als in anderen. Außerdem würde sich jede Radiumaufnahme primär im Knochen ablagern und Radon-Folgeprodukte primär in der Lunge. Die Zahl der Toten aus allen Krebsarten kombiniert lag in Karnes County ebenfalls nicht höher. Die RRs der Krebssterblichkeit in Karnes County *vor* und in den ersten Jahren des Betriebs (1950–64), kurz nach Beginn der Uranaktivitäten (1965–79) und in den beiden Zeiträumen (1980–89, 1990–2001) waren ähnlich: 1,0, 0,9, 1,1 bzw. 1,0. Keine ungewöhnlichen Muster der Krebssterblichkeit wurden in Karnes County über einen Zeitraum von 50 Jahren beobachtet; dies deutet darauf hin, dass Uranabbau und—verarbeitung nicht zu einer Zunahme der Krebsraten unter den Bewohnern führte.

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Appendix 6

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Cancer and Noncancer Mortality in Populations Living Near Uranium and Vanadium Mining and Milling Operations in Montrose County, Colorado, 1950–2000

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Boice, J. D., Jr., Mumma, M. T. and Blot, W. J. Cancer and Noncancer Mortality in Populations Living Near Uranium and Vanadium Mining and Milling Operations in Montrose County, Colorado, 1950–2000. *Radiat. Res.* 167, 711–726 (2007).

Mining and milling of uranium in Montrose County on the Western Slope of Colorado began in the early 1900s and continued until the early 1980s. To evaluate the possible impact of these activities on the health of communities living on the Colorado Plateau, mortality rates between 1950 and 2000 among Montrose County residents were compared to rates among residents in five similar counties in Colorado. Standardized mortality ratios (SMRs) were computed as the ratio of observed numbers of deaths in Montrose County to the expected numbers of deaths based on mortality rates in the general populations of Colorado and the United States. Relative risks (RRs) were computed as the ratio of the SMRs for Montrose County to the SMRs for the five comparison counties. Between 1950 and 2000, a total of 1,877 cancer deaths occurred in the population residing in Montrose County, compared with 1,903 expected based on general population rates for Colorado (SMR_{CO} 0.99). There were 11,837 cancer deaths in the five comparison counties during the same 51-year period compared with 12,135 expected (SMR_{CO} 0.98). There was no difference between the total cancer mortality rates in Montrose County and those in the comparison counties (RR = 1.01; 95% CI 0.96–1.06). Except for lung cancer among males (RR = 1.19; 95% CI 1.06–1.33), no statistically significant excesses were seen for any causes of death of *a priori* interest: cancers of the breast, kidney, liver, bone, or childhood cancer, leukemia, non-Hodgkin lymphoma, renal disease or nonmalignant respiratory disease. Lung cancer among females was decreased (RR = 0.83; 95% CI 0.67–1.02). The absence of elevated mortality rates of cancer in Montrose County over a period of 51 years suggests that the historical milling and mining operations did not adversely affect the health of Montrose County residents. Although descriptive correlation analyses such as this preclude definitive causal inferences, the increased lung cancer mortality seen among males but not females is most likely due to prior occupational exposure to radon and cigarette smoking among underground miners residing in Montrose County, consistent with previous cohort studies of Colorado miners and of residents of the town of Uravan in Montrose County. © 2007 by Radiation Research Society

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INTRODUCTION

Uranium and vanadium oxides were extracted from carnotite ore as early as 1900 in Montrose County, CO (*1*). In 1912, carnotite ore was mined and radium was extracted at one of the first mills in what later became the town of Uravan, Montrose County, on the Western Slope of Colorado (*2, 3*). By 1919, the mining of uranium was well established as an ongoing industry in Montrose Country (*1*). Between 1925–1945, carnotite ore was mined to extract vanadium for use as a hardening component of steel. Some uranium was also extracted for use in ceramic and chemical industries. In the mid to late 1930s, the U.S. Vanadium Corporation built a mill at Uravan, named from the first three letters of the elements uranium and vanadium. During the 1940s ore was mined and milled in Montrose County to extract uranium for use in the Manhattan Project to produce the first atomic weapons (*2*). According to the U.S. Geological Survey (*5*), there were more uranium mines located in Montrose County (n = 223) than in any other county in Colorado. The average density of about one mine per 10 square miles was also the highest in Colorado. Mining and milling activities were substantially curtailed by the 1980s for economic reasons (*2, 4*).

The extraction of uranium from ore produced solid and liquid wastes, called tailings. The wastes contained the naturally occurring radionuclides present in the ore, including thorium, radium and other decay products. Tailing piles, runoff collection ponds, ore transport, and airborne and liquid effluents from the mills (extraction facilities) were potential sources of environmental exposure to humans (*6*). Historical milling and mining activities have raised questions over the years about possible increased exposure of milling and mining communities to ionizing radiation from

uranium and its decay products, possible contamination of groundwater and vegetation, and possible increased levels of indoor radon.

The primary occupational exposures in uranium mills were to airborne uranium, silica and vanadium. NIOSH conducted a comprehensive study of 1,484 men who worked at one of seven uranium mills on the Colorado Plateau on or after January 1, 1940 (*7*). Increased numbers of deaths were found for nonmalignant respiratory diseases, lung cancer, lymphoma and kidney disease. The authors were unable to show conclusively whether these deaths resulted from working in the mills because length of employment was not associated with increased risks. Studies of other "non-mining" uranium workers have provided little to no evidence of increased cancer risks among occupationally exposed workers (*8–10*). Environmental studies of populations residing in areas near uranium mining, milling or processing facilities similarly have not shown increased cancer risks (*11–13*). Studies of populations with increased levels of uranium, radium, radon and other radionuclides in drinking water also have not found associations with any cancers, overt kidney disease or bone disease (*14–19*).

An earlier cohort study of over 3,500 residents of the town of Uravan in Montrose County (which contained one of the earliest uranium and vanadium mills in the country) found no statistically significant increases in cancer mortality or cancer incidence except for male lung cancer, which was attributed to prior employment of some residents in underground uranium mines and increased tobacco use (*20*). This explanation was plausible since underground miners working on the Colorado Plateau are known to have been exposed to high cumulative levels of radon gas and radon decay products during their working careers and to have been heavy smokers (*21, 22*). While underground miner studies have linked radon exposures and tobacco use to increased lung cancer risks, no other cancer has been reported to be significantly linked to radon concentrations among underground miners (*23–25*). Studies of underground miners of the Colorado Plateau, however, have reported significant elevations of noncancer deaths from tuberculosis, nonmalignant respiratory disease and accidents (*24*).

Radium (which naturally occurs in carnotite ore but is not extracted during the milling of uranium and vanadium) is a component of mill tailings. Excessive ingestion of radium has been linked to bone cancer in occupational studies, although only at extraordinarily high levels, and no other cancer excesses were observed except for a rare carcinoma of the paranasal sinuses (*26, 27*). Radium decays into radon, and radon levels are increased near mill tailings. Case-control studies of indoor radon suggest increased lung cancer rates in long-term residents of homes with high radon concentrations (*25, 28, 29*) but have not found increased rates of childhood leukemia or childhood cancer (*30–32*). Radium also decays by emitting γ radiation, and excessive exposure to such external penetrating radiation is a known cause of breast cancer, leukemia and other malignancies (*33–35*). Cohort studies of uranium processors, millers and miners, however, have revealed no significant increases in leukemia, nor have descriptive studies of communities living near uranium milling and processing facilities revealed significant increases (*7, 8, 11, 12, 25*). Some ecological studies have reported correlations between radon levels and leukemia, but results are not consistent, and some studies appeared methodologically flawed (*25, 36*). Two cohort studies of underground miners have reported increases in leukemia, but the risks were not significant, nor were they correlated with cumulative radon exposures (*37, 38*). A recent case-control study of leukemia among Czech uranium miners reported a significant association with radon concentrations for chronic lymphocytic leukemia, a cancer that is not considered inducible by radiation (*39*), suggesting that aspects in the mining environment other than radon might be involved (*37, 40*).

Vanadium also was extracted from carnotite ore and is another source of potential exposure. No human study has linked vanadium to increased cancer rates (*41*), but recent animal experiments have found significant elevations of lung cancer in rats (*42*).

An earlier cancer mortality study of counties in the Western Slope of Colorado by the National Cancer Institute revealed no unusual patterns of death compared to the rest of Colorado (*43*). A later tabulation of county cancer mortality rates for 1950–1979 suggested increased rates of male lung cancer in Montrose County compared to the state of Colorado, but female lung and breast cancer rates were decreased, as were leukemia rates (*44*). Because of the long history of uranium and vanadium milling and mining activities and the large number of uranium mines in Montrose County, we extended the previous county cancer mortality studies by 20 years and compared the mortality risks in Montrose County with the mortality risks seen in demographically similar counties in Colorado as well as with the state of Colorado and the United States. Further, we evaluated noncancer causes of death in Montrose County, which had not previously been done.

METHOD

Cancer and noncancer mortality rates among Montrose county residents were compared with rates among residents in five other counties in Colorado that were selected because of similar demographic and socioeconomic characteristics. Mortality rates in Montrose County also were compared to the mortality rates in the general populations of Colorado and the United States, and standardized mortality ratios (SMRs) were computed. Following an approach taken by the National Cancer Institute (NCI) in a nationwide study of cancer mortality in counties with nuclear installations, relative risks were estimated as the ratio of the SMRs for Montrose County to the SMRs for the comparison counties (*45*). Similar approaches have been used to evaluate cancer risk in communities living in areas near uranium mining, milling and processing operations in Colorado, Pennsylvania and Texas (*11, 13, 43*).

TABLE 1
Demographic and Socioeconomic Characteristics of Montrose County, the Comparison Counties[a] and the State of Colorado

County	Total score[a]	Total persons	Area (square miles)	Population density	Percentage							Median household income ($)
					Male	White	Rural	High school graduate	Age 65+	Employed	Below poverty	
Study county												
Montrose	—	24,423	2,242	10.9	48.4	96.0	63.7	73.4	16.4	57.2	14.0	22,610
Comparison counties[a]												
Montezuma	177	18,672	2,040	9.2	48.6	85.1	61.0	73.6	12.3	57.3	20.0	22,491
Delta	181	20,980	1,148	18.4	49.1	96.0	81.9	72.4	22.3	45.3	17.4	18,532
Yuma	186	8,954	2,369	3.8	48.9	98.5	69.6	77.7	16.8	59.9	13.1	22,249
Logan	204	17,567	1,845	9.6	48.5	95.8	41.0	79.1	15.4	64.1	14.5	22,065
Mesa	214	93,145	3,341	28.0	48.4	94.9	18.4	79.0	14.4	58.2	14.8	23,698
Total comparison counties	—	159,318	10,743	14.9	48.5	94.2	37.1	77.4	15.4	57.1	15.6	22,570
State of Colorado		3,294,394	103,718	31.8	49.5	88.3	17.6	83.8	10.0	66.4	11.4	30,140

[a] As described in the Methods, a simple rank-sum algorithm was applied to all Colorado counties contrasting demographic and socioeconomic characteristics with those of Montrose County. A low score signifies close similarity to Montrose County. The five counties most similar to Montrose County (i.e., with the lowest scores) were selected as comparison counties.

Mortality Data

Counties are the smallest areas for which both population estimates and annual counts of the number of deaths from specific causes are readily available back to 1950 from the National Center for Health Statistics (*46*). Cancer mortality data for all counties in the state of Colorado from 1950 to 2000 were obtained from the National Cancer Institute (*46*). Noncancer mortality rates for counties in Colorado from 1960 to 1999 were obtained from the University of Pittsburgh (*47*). The number of deaths from noncancer causes was not available and was estimated by multiplying the cause-specific mortality rates by the corresponding age, sex, race and calendar year population data available from the National Cancer Institute (*46*).

Selection of Comparison Counties

Mining and milling activities in Montrose County began in the early 1900s; this county had many more uranium mines and mills than any other Colorado county (*5*). Accordingly, Montrose County was chosen as the study county. Comparison counties were selected based on similar population characteristics. All 62 of Colorado's other counties were eligible for selection as comparison counties. Census Bureau demographic data on nine socioeconomic variables were obtained for all counties, i.e., population density (total residents divided by county area), percentage male, percentage white, percentage rural, percentage high school graduate, percentage over age 64 years, percentage employed, percentage below poverty, and median household income (*48*). For each of these characteristics, counties were sorted and ranked based on their similarity to Montrose County. The rank values for the nine socioeconomic variables were then summed, with a low sum (or score) representing more similarity to Montrose than a high sum (or score). The five counties with the lowest scores (Montezuma, Delta, Yuma, Logan and Mesa) were chosen as the comparison counties (Table 1, Fig. 1). The determination of a socioeconomic score based on area-level characteristics is similar to that done in other studies (*49*). Data on diet, smoking and other potential risk factors for disease are not readily available at the county level, but use of comparison counties in proximity to Montrose County (Montezuma, Delta and Mesa) should help minimize differences in these unknown factors, assuming that factors such as diet would be similar in neighboring areas. Montrose County had the highest number of uranium mines (n = 223) of any county in Colorado. Delta and Yuma Counties did not have any uranium mines, Logan had one, Montezuma had eight, and Mesa had 55 (*5*). The average density of mines in the five comparison counties was about six per 1000 square miles or 600 times less than Montrose County. Montrose County had two operating uranium mills, Mesa Country had one, and the other comparison counties had none. Supplemental analyses excluding Mesa County were conducted to reduce the likelihood that these mining and milling activities had affected the mortality rates in the comparison counties.

Statistical Analyses

Mortality rates for the general populations of Colorado and the United States were used for calculating expected numbers of deaths and SMRs among the Montrose County and comparison county populations. Counts of cancer deaths by cause, sex, race and 5-year age group were obtained for Montrose County and the five comparison counties for each year from 1950 to 2000. For each type of cancer and each county, the expected number of deaths, based on concurrent Colorado and U.S. experience, was calculated for the 51-year study period (*46, 47*). Expected numbers were obtained by multiplying annual Colorado and U.S. cancer death rates by the estimated populations, stratified by 5-year age group, race and sex. Counts of observed and expected deaths were then summed over the periods 1950–1969, 1970–1984 and 1985–2000. These intervals were selected to be of similar size, and consideration was given to the fact that practically all milling and mining activities had ceased by 1985.

The standardized mortality ratio was calculated by dividing the number of deaths observed among the Montrose County population by the number of deaths that would be expected using U.S. (SMR_{US}) or Colorado (SMR_{CO}) rates. Relative risks (RRs) were computed as the ratios of the SMRs for Montrose County to the comparison counties, and 95% confidence intervals were calculated following the methods applied in the NCI nationwide study of nuclear facilities (*45*). A 95% confidence interval that contains 1.00 means that chance cannot be ruled out as a possible explanation for any observed differences in mortality rates between Montrose County and the comparison counties. When a 95% confidence interval does not contain 1.00, the difference in mortality rates is called "statistically significant" and means that chance is not a likely explanation for the observed results (*50*).

SMRs and RRs for noncancer deaths between 1960 and 1999 were computed in a similar manner as for cancer deaths. Although counts of noncancer deaths were not available, they could be estimated accurately

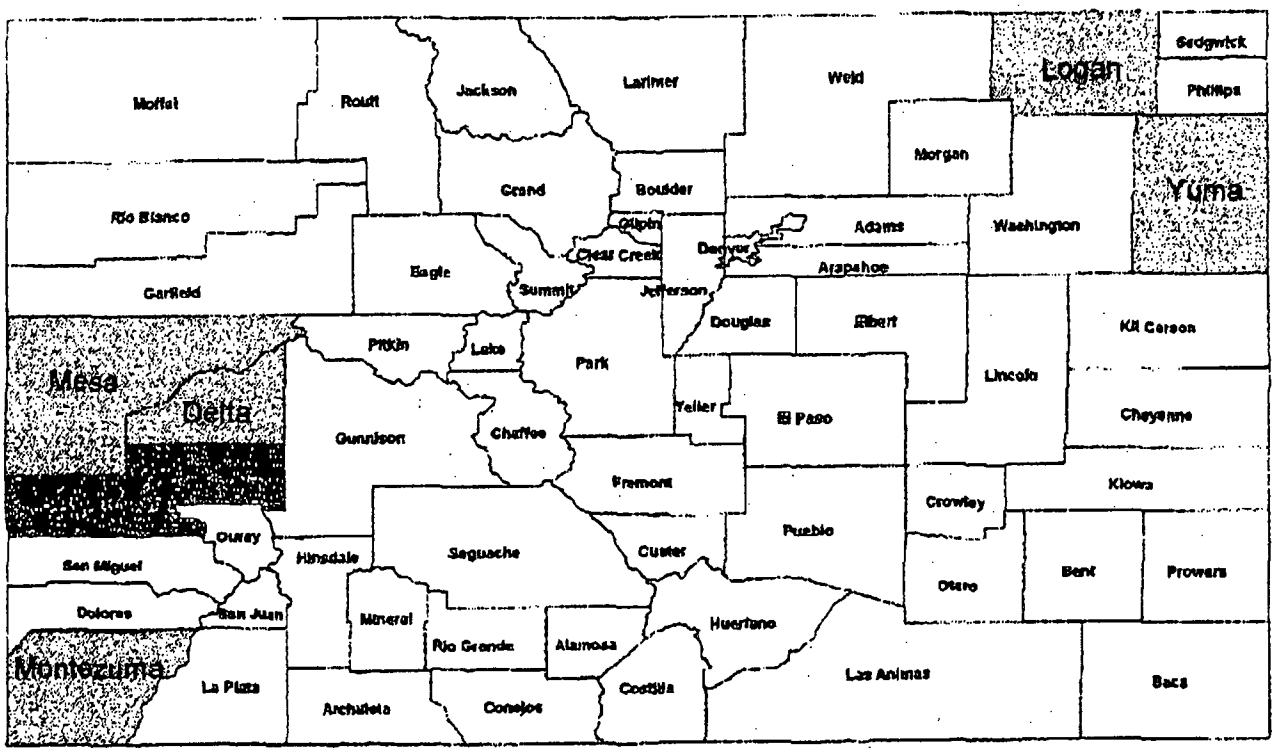

FIG. 1. County map of Colorado indicating the study county (Montrose) and the comparison counties (Mesa, Delta, Montezuma, Logan and Yuma) selected to be similar to Montrose County on demographic and socioeconomic characteristics.

by multiplying the age, calendar year, sex, race and site-specific mortality rates times the corresponding population data obtained from the NCI. This procedure was validated by comparing the estimated counts for cancer deaths with the actual counts of cancer deaths available from the NCI data files (*46*).

While the study uses existing databases that contain no identifying information, strata containing two or fewer deaths are not presented but are listed as LT3 to denote "less than three". This is to abide by the confidentiality requirements for using the NCI and National Center for Health Statistics databases. The concern is the possibility that individuals with certain characteristics might be identified if the number of deaths were small.

RESULTS

The number of residents in Montrose County and the five comparison counties totaled 24,423 and 159,318, respectively, in 1990 (Table 1). Residents in the comparison counties were similar to residents in Montrose County with regard to demographic indicators of cancer risk such as age, race and various accepted measures of socioeconomic status such as educational level and median household income. Most of the population studied was white with few black or Asian citizens; 15.4% of the comparison county residents were older than 64 years compared to 16.4% for Montrose County residents; most graduated from high school (77.4% compared to 73.4%), and most were employed (57.1% compared to 57.2%). The median household incomes of Montrose County ($22,610) and the comparison counties ($22,570) were also similar. Comparison counties were less rural (37.1% compared to 63.7%) than Montrose County, but residents were similar with regard to poverty level (15.6% compared to 14.0%). Montrose and the comparison counties differed from the state of Colorado in being more rural, less educated, older and much less affluent. Because certain diseases are known to be associated with low socioeconomic status (*51, 52*), any differences in mortality risks based on Colorado comparisons may be related in part to differences in socioeconomic factors and not environmental factors. Any bias associated with differences in socioeconomic status would be in the direction of producing higher SMRs. Some variations in characteristics were also seen among the comparison counties (e.g., Yuma has a relatively low population density and Mesa has a high population density). Such differences, however, are balanced by closer similarities in other characteristics (e.g., Yuma is similar to Montrose in rural characteristics and Mesa is similar in poverty characteristics).

Table 2 presents the total number of cancer deaths, SMRs based on Colorado and U.S. rates, and RRs comparing Montrose County with the comparison counties, for all cancers and for specific cancers, during 1950–2000. There were no significantly increased or significantly decreased RRs for any cancer or combination of cancers. No significant differences were seen for all cancers (RR 1.01; 95% CI 0.96–1.06), lung cancer (RR 1.08; 95% CI 0.98–1.19),

kidney and liver cancer (RR 0.92; 95% CI 0.74–1.15), breast cancer (RR 0.86; 95% CI 0.71–1.03), non-Hodgkin lymphoma (RR 1.05; 95% CI 0.82–1.34), leukemia (RR 0.78; 95% CI 0.60–1.01), or childhood cancer (RR 0.73; 95% CI 0.43–1.25).

Overall, results based on Colorado population rates were generally similar to results based on the comparison counties (e.g., the SMR_{CO} for all cancer deaths was 0.99 based on Colorado rates, whereas the RR was 1.01 contrasting cancer rates in Montrose with the comparison counties). There were 1,877 cancer deaths in Montrose County (SMR_{CO} 0.99) and 11,837 cancer deaths in the comparison counties (SMR_{CO} 0.98). The most frequent causes of death in Montrose County and the comparison counties were cancer of the lung (SMR_{CO} 1.14 compared to. 1.06), breast (SMR_{CO} 0.80 compared to 0.93), colon and rectum (SMR_{CO} 0.88 compared to 0.93), and prostate (SMR_{CO} 1.07 compared to 1.00). Leukemia deaths occurred below expectation in both Montrose County and the comparison counties (SMR_{CO} 0.73 compared to 0.94). There were five childhood leukemia deaths in Montrose County and 58 in the comparison counties (SMR_{CO} 0.57 compared to 1.14). The SMRs based on U.S. rates were generally lower than those based on Colorado rates (e.g., the all-cancer SMR_{US} of 0.85 was significantly lower than the all-cancer SMR_{CO} of 0.99 based on Colorado rates). Similarly, the lung cancer SMR_{US} of 0.85 based on U.S. rates was significantly low, whereas the SMR_{CO} of 1.14 based on Colorado rates was significantly high.

Contrasting cancer rates in Montrose with the comparison counties revealed no significantly high or significantly low relative risks for any cancer of *a priori* interest. Slight elevations were seen for cancers of the lung (RR 1.08; 95% CI 0.98–1.19), bone (RR 1.36; 95% CI 0.63–2.91), and non-Hodgkin lymphoma (RR 1.05; 95% CI 0.82–1.34). Slight deficits were seen for cancers of the kidney (RR 0.80; 95% CI 0.56–1.14), breast (RR 0.87; 95% CI 0.72–1.04), thyroid (RR 0.82; 95% CI 0.32–2.07), leukemia other than CLL (RR 0.80; 95% CI 0.61–1.06), and childhood cancer (RR 0.73; 95% CI 0.43–1.25).

Of the 28 relative risks presented, 16 were less than 1.00 and 12 were greater than 1.00, a distribution about the overall value of 1.01 for all cancers combined that is consistent with the play of chance when evaluating so many individual cancers. SMRs based on comparisons with the Colorado population were similar to the RRs in magnitude and direction (i.e., above or below 1.00). For all cancers taken together, the SMR_{CO} for men and women combined was 0.99 (95% CI 0.94–1.03) based on Colorado rates and similar to the RR of 1.01 (95% CI 0.96–1.06) based on the comparison counties.

With regard to sex-specific risks, there were no significantly high or significantly low RRs for female residents of Montrose County (Table 3). Overall, female cancer mortality rates in Montrose County were the same as those in the comparison counties (RR 1.00; 95% CI 0.93–1.08). Lung cancer (RR 0.83; 95% CI 0.67–1.02) and breast cancer (RR 0.86; 95% CI 0.72–1.04) risks were notably low, with the deficits approaching statistical significance. The overall cancer rates for males in Montrose County were also similar to those in the comparison counties (RR 1.02; 95% CI 0.95–1.09). Lung cancer, however, was significantly increased (RR 1.19; 95% CI 1.06–1.33), whereas kidney cancer (RR 0.60; 95% CI 0.37–0.99), liver and kidney cancer (RR 0.70; 95% CI 0.50–0.97), and leukemia (RR 0.63; 95% CI 0.44–0.90) were significantly decreased. The SMRs based on Colorado rates were extremely similar to the RRs based on the comparison counties, indicating that the choice of the referent made little difference.

Table 4 presents, for both sexes combined, the SMRs and RRs of mortality for selected cancers in Montrose County for three periods during 1950–2000. Overall, cancer rates in Montrose County were similar to those in the comparison counties. No RR for any cancer was significantly above or below expectation for any time interval. There were no increasing patterns of risk over the 51-year period of observation. There was a tendency for the SMRs and the RRs to be lower in the last interval, 1985–2000.

Table 5 presents SMRs and RRs for noncancer causes of death for the years 1960–1999. A slightly increased RR for all causes of death (RR 1.03; 95% CI 1.01–1.06) compared to the five comparison counties was due largely to a significant increase in deaths from accidents other than automobile accidents (RR 1.15; 95% CI 1.02–1.30). Deaths due to tuberculosis were also significantly increased (RR 1.89; 95% CI 1.10–3.48). Significantly low RRs were seen for hypertension but not for heart disease. Of the 23 RRs presented in Table 5, 10 were below, 11 were above, and two were equal to the central value of 1.03, which is consistent with the play of chance when many comparisons are made.

SMRs based on U.S. rates tended to be lower than those based on Colorado rates. The all-causes-of-death SMR_{US} for Montrose County residents based on U.S. rates, for example, was significantly low. Lower SMRs based on U.S. rates were also seen for heart disease and cerebrovascular disease, but significantly higher mortality rates were seen for nonmalignant respiratory disease, accidents and suicides. These differences were also apparent among residents of the five comparison counties and may reflect differences in socioeconomic factors between the study counties and the general populations of the state of Colorado and the United States (*52*).

Table 6 presents, for both sexes combined, the SMRs and RRs for selected noncancer causes of death in Montrose County for three periods during 1960–1999. There was little tendency for any cause of death to increase over time. The RRs tended to be higher in the earliest interval, 1960–1969, than in any other interval. The all-cause RR was significantly high during 1960–1969 (RR 1.14) whereas it was close to expectation during 1970–1984 (RR 1.02) and 1985–1999 (RR 1.01). The significantly high all-cause RR during 1960–1969 was due to significantly high risks for

TABLE 2
Observed (Obs) and Expected (Exp)[a] Numbers of Cancer Deaths and Standardized Mortality Ratios (SMRs) for Montrose County and the Five Comparison Counties during 1950–2000, and the Estimates of Relative Risk (RR)[b]

	Montrose County				
Cancer (ICD 9)	Obs	Exp_{US}	Exp_{CO}	SMR_{US}	SMR_{CO}
All cancers (140–208)	1,877	2,201.4	1,903.2	0.85*	0.99
Esophagus (150)	22	39.4	31.3	0.56*	0.70
Stomach (151)	87	88.6	80.3	0.98	1.08
Colon/rectum (153, 154)	207	279.7	234.0	0.74*	0.88
Pancreas (157)	121	111.8	107.0	1.08	1.13
Lung (162)	454	531.0	397.5	0.85*	1.14*
Skin (172, 173)	37	38.0	37.7	0.97	0.98
Malignant melanoma of the skin (172)	25	26.7	27.7	0.94	0.90
Breast (174)	126	175.5	158.2	0.72*	0.80*
Cervix uteri (180)	15	26.8	25.0	0.56*	0.60
Corpus uteri (182)	34	29.7	24.4	1.15	1.39
Ovary (183)	49	56.2	54.0	0.87	0.91
Prostate (185)	148	136.3	138.2	1.09	1.07
Urinary bladder (188)	44	57.1	48.4	0.77	0.91
Kidney (189)	34	45.1	41.9	0.75	0.81
Liver and kidney (155, 189)	88	106.3	95.9	0.83	0.92
Bone (170)	8	8.4	6.4	0.95	1.25
Connective tissue (171)	12	11.9	12.0	1.01	1.00
Brain & CNS (191, 192)	44	52.1	49.3	0.84	0.89
Thyroid (193)	5	5.7	5.6	0.88	0.89
Non-Hodgkin lymphoma (200, 202)	75	76.4	72.6	0.98	1.03
Hodgkin lymphoma (201)	15	12.8	11.1	1.17	1.35
Multiple myeloma (203)	33	32.3	32.9	1.02	1.00
Leukemia (204–208)	65	91.4	88.6	0.71*	0.73*
Leukemia, CLL (204.1)[c]	10	13.3	13.1	0.75	0.76
Leukemia, not CLL	55	77.1	74.8	0.71*	0.74*
Childhood leukemia (<20 years)	5	9.0	8.8	0.55	0.57
Childhood cancer (<20 years)	15	21.9	20.1	0.68	0.75

[a] Expected numbers based on U.S. rates (Exp_{US}) and on Colorado rates (Exp_{CO}).
[b] RR is taken as the SMR_{CO} for Montrose County divided by the SMR_{CO} for the comparison counties.
[c] CLL denotes chronic lymphocytic leukemia.
* $P < 0.05$.

tuberculosis (RR 3.07), diabetes (RR 1.90), cerebrovascular disease (RR 1.22), cirrhosis of the liver (RR 1.91), and all external causes of death (RR 1.20). Except for tuberculosis, none of these causes of death were significantly elevated overall or during 1970–1984 or 1985–1999. For the interval 1970–1984, the RR (1.04) and estimated number of all-cancer deaths (n = 508) were the same as those computed in Table 4 based on exact cancer counts; this concordance supports the validity of the approach used to estimate RRs for the noncancer deaths.

DISCUSSION

Cancer and noncancer mortality rates among residents of Montrose County were similar to those of residents in the state of Colorado as well as residents in five comparison counties in Colorado selected as comparable based on a wide range of demographic and socioeconomic characteristics. Notably, no significant increases were seen for either men or women for all cancers combined, kidney cancer or kidney disease, liver cancer or bone cancer, leukemia, lymphoma or nonmalignant respiratory disease. These causes of death were of an *a priori* interest because of associations reported previously in studies of uranium mill workers and uranium miners of the Colorado Plateau (*7, 24*) or because they are the most biologically plausible tissues to be affected by any deposition of uranium and its decay products after possible ingestion or inhalation (*53, 54*). Significant increases among men but not women, however, were seen for lung cancer, tuberculosis and accidental injuries. These causes of death were also previously reported to be significantly increased among male miners of the Colorado Plateau (*24*) and suggest that the mortality rates in Montrose County were influenced by occupational rather than environmental factors since it is implausible that environmental exposures would affect the mortality rates of these three causes of death in one sex but not in the other. Tobacco use likely contributed to this risk of lung cancer since miners of the Colorado Plateau are known to be heavy smokers (*22*). Although there were increases and decreases in other causes of death over time, there were no consistent patterns to suggest that living in Montrose County increased the risk

TABLE 2
Extended

Comparison counties						
Obs	Exp_{US}	Exp_{CO}	SMR_{US}	SMR_{CO}	RR[a]	95% CI
11,837	13,981.4	12,135.3	0.85*	0.98	1.01	0.96–1.06
196	247.1	195.4	0.79*	1.00	0.70	0.45–1.09
496	581.0	527.4	0.85*	0.94	1.15	0.92–1.45
1,416	1,814.8	1,519.7	0.78*	0.93	0.95	0.82–1.10
705	715.3	685.6	0.99	1.03	1.10	0.91–1.33
2,612	3,282.0	2,472.7	0.80*	1.06	1.08	0.98–1.19
218	237.0	235.3	0.92	0.93	1.06	0.75–1.50
171	164.5	171.4	1.04	1.00	0.90	0.59–1.38
951	1,133.7	1,025.9	0.84*	0.93	0.86	0.71–1.03
136	176.5	165.6	0.77*	0.82	0.73	0.43–1.24
168	197.4	163.4	0.85	1.03	1.35	0.94–1.96
337	363.6	350.3	0.93	0.96	0.94	0.70–1.27
881	865.6	882.1	1.02	1.00	1.07	0.90–1.28
281	369.2	312.9	0.76*	0.90	1.01	0.74–1.39
270	282.8	264.9	0.95	1.02	0.80	0.56–1.14
613	679.8	615.2	0.90	1.00	0.92	0.74–1.15
38	53.9	41.3	0.70	0.92	1.36	0.63–2.91
58	73.9	75.6	0.78	0.77	1.30	0.70 2.42
291	320.0	302.7	0.91	0.96	0.93	0.68–1.28
40	37.2	36.7	1.07	1.09	0.82	0.32–2.07
451	479.9	457.4	0.94	0.99	1.05	0.82–1.34
55	80.9	70.0	0.68*	0.79	1.72	0.97–3.04
217	204.0	209.5	1.06	1.04	0.97	0.67–1.39
530	578.9	560.9	0.92	0.94	0.78	0.60–1.01
90	84.1	83.2	1.07	1.08	0.71	0.37–1.36
434	489.8	473.8	0.89	0.92	0.80	0.61–1.06
58	52.3	50.7	1.11	1.14	0.50	0.20–1.24
120	128.8	117.6	0.93	1.02	0.73	0.43–1.25

of cancer or other fatal diseases other than those related to employment as an underground miner and increased tobacco use. This is one of the few descriptive county mortality studies that included both cancer and noncancer mortality, and the male excess of specific cancer and noncancer diseases that have been associated with underground mining (i.e., lung cancer, tuberculosis and accidental deaths) strengthens the inference made that occupational exposures and cigarette smoking were responsible for the observed county excesses.

Lung Cancer

Given the statistically significant increase in lung cancer rates among men living in Montrose County, we considered the possibility that environmental exposures from uranium and vanadium milling and mining activities might be contributing factors. This is unlikely, however, because the risk of lung cancer was decreased in women (RR 0.82), and it is implausible that an environmental exposure would increase the risk of lung cancer among men and decrease the risk of lung cancer among women. Further, it has been known for some time that working as an underground miner in the Colorado Plateau is associated with an increased rate of lung cancer due to high-level exposure to radon and its decay products, increased tobacco use and possibly other mine exposures such as silica, diesel exhaust and blasting fumes (*21, 22, 24*). It has also been reported that radon exposures and cigarette smoking among underground miners of the Colorado Plateau have interacted in a synergistic or nearly multiplicative fashion to increase lung cancer risks. It is noteworthy that a previous study of persons living in the town of Uravan in Montrose County found a significant increase in lung cancer among men but not women, which was also attributed to employment in underground mines and smoking and not to environmental exposures (*20*).

Because workers with a specific occupation usually make up only a small percentage of all persons residing in a county, it is often difficult to identify occupational risks based on county mortality studies. However, there are notable examples where this has been possible [e.g., occupational exposure to asbestos from shipyard work during World War II was identified as a risk factor for lung cancer based on county mortality data and later confirmed in analytic studies (*55*)]. Indirect support for the likelihood that our county mortality study identified an occupational rather than environmental cause of male lung cancer also comes from the similarities in other causes of death that were elevated both

TABLE 3
Observed (Obs)[a] Numbers of Cancer Deaths and Standardized Mortality Ratios (SMRs) for Montrose County for Males and Females during 1950–2000, and the Estimates of Relative Risk (RR)[b]

	Males					Females				
Cancer (ICD 9)	Obs[a]	SMR_{US}	SMR_{co}	RR[b]	95% CI	Obs[a]	SMR_{US}	SMR_{co}	RR[b]	95% CI
All cancers (140–208)	1,068	0.85*	1.02	1.02	0.95–1.09	809	0.85*	0.95	1.00	0.93–1.08
Esophagus (150)	16	0.52*	0.65	0.63	0.37–1.05	6	0.69	0.87	1.01	0.43–2.38
Stomach (151)	63	1.10	1.21	1.30	0.99–1.70	24	0.77	0.85	0.89	0.58–1.37
Colon/rectum (153, 154)	108	0.72*	0.90	0.97	0.79–1.19	99	0.76*	0.86	0.93	0.75–1.14
Pancreas (157)	64	1.02	1.08	0.99	0.76–1.28	57	1.16	1.20	1.26	0.95–1.67
Lung (162)	353	0.94	1.27*	1.19*	1.06–1.33	101	0.66*	0.84	0.83	0.67–1.02
Skin (172, 173)	24	0.98	1.00	1.06	0.69–1.64	13	0.96	0.95	1.05	0.59–1.89
Malignant melanoma of the skin (172)	16	0.97	0.94	0.97	0.57–1.64	9	0.90	0.84	0.81	0.40–1.62
Breast (174)	—	—	—	—	—	126	0.72*	0.80*	0.86	0.72–1.04
Cervix uteri (180)	—	—	—	—	—	15	0.56*	0.60*	0.73	0.43–1.24
Corpus uteri (182)	—	—	—	—	—	34	1.15	1.39	1.35	0.94–1.96
Ovary (183)	—	—	—	—	—	49	0.87	0.91	0.94	0.70–1.27
Prostate (185)	148	1.09	1.07	1.07	0.90–1.28	—	—	—	—	—
Urinary bladder (188)	29	0.70	0.84	0.97	0.65–1.43	15	0.97	1.09	1.12	0.65–1.93
Kidney (189)	17	0.58*	0.64	0.60*	0.37–0.99	17	1.08	1.10	1.16	0.69–1.94
Liver and kidney (155, 189)	39	0.63*	0.72*	0.70*	0.50–0.97	49	1.11	1.17	1.23	0.91–1.67
Bone (170)	6	1.19	1.55	1.74	0.71–4.29	LT3	0.60	0.79	0.82	0.19–3.56
Connective tissue (171)	5	0.80	0.79	1.06	0.41–2.75	7	1.27	1.23	1.55	0.68–3.53
Brain and CNS (191, 192)	23	0.76	0.81	0.83	0.54–1.29	21	0.96	1.00	1.06	0.67–1.69
Thyroid (193)	LT3	0.44	0.46	0.42	0.06–3.15	4	1.19	1.16	1.07	0.37–3.08
Non-Hodgkin lymphoma (200, 202)	32	0.75	0.82	0.81	0.56–1.18	43	1.28	1.29	1.33	0.96–1.85
Hodgkin lymphoma (201)	7	0.89	0.98	1.49	0.65–3.41	8	1.63	2.00	1.99	0.90–4.40
Multiple myeloma (203)	18	1.00	0.99	0.92	0.56–1.50	15	1.05	1.02	1.03	0.60–1.78
Leukemia (204–208)	32	0.59*	0.61*	0.63*	0.44–0.90	33	0.89	0.92	1.01	0.70–1.46
Leukemia, CLL (204.1)[c]	6	0.73	0.72	0.61	0.26–1.41	4	0.80	0.84	0.91	0.32–2.59
Leukemia, not CLL	26	0.57*	0.59*	0.64*	0.43–0.96	29	0.92	0.94	1.03	0.70–1.53
Childhood leukemia (<20 years)	LT3	0.19	0.20	0.19	0.03–1.37	4	1.07	1.05	0.86	0.30–2.45
Childhood cancer (<20 years)	6	0.47	0.52	0.51	0.22–1.17	9	0.97	1.06	1.03	0.51–2.10

[a] Observed number of cancer deaths in Montrose County. LT3 denotes less than 3 deaths.
[b] RR is taken as the SMR_{co} for Montrose County divided by the SMR_{co} for the comparison counties.
[c] CLL denotes chronic lymphocytic leukemia.
* $P < 0.05$.

among miners of the Colorado Plateau and among Montrose County residents (i.e., tuberculosis and accidental deaths were significantly increased among miners and also among male, but not female, residents of Montrose County).

Smoking

Cigarette smoking is the predominant cause of lung cancer and is responsible for more than 87% of all lung cancers diagnosed in the United States (*56*). It is thus possible that men in Montrose County used tobacco products to a greater extent than men who lived in other counties in Colorado. This supposition seems possible since miners of the Colorado Plateau are known to be heavy smokers (*22*). Females residing in Montrose County had a lower risk of lung cancer than females residing in the comparison counties or the state of Colorado. Although this suggests that they may have smoked proportionally less than females in the comparison counties, the lower risk was not significant and thus chance cannot be ruled out. Further, the risk of other smoking-related sites among females, such as the bladder and pancreas, was slightly elevated and in the opposite direction expected if they were infrequent smokers.

External Radiation

The potential for environmental exposures to penetrating radiation, such as γ rays, to have contributed to the risk of cancer in Montrose County residents is also unlikely because of the deficits seen for leukemia, female breast cancer and childhood cancer. Leukemia and female breast cancer are the cancers most frequently observed to be increased in comprehensive epidemiological studies of populations exposed to excessive amounts of ionizing radiation, and, in addition, children are considered to be at higher risk of radiation-induced cancers than adults (*33–35*). Living in areas of high natural background radiation, which primarily would include exposure to external radiation, also has not been convincingly linked to elevations in cancer risk or thyroid disease (*57, 58*).

Uranium Ingestion

Uranium from the environment can enter the body by ingestion of food and water or by inhalation of uranium

TABLE 4
Standardized Mortality Ratios (SMR) and Relative Risks (RRs) for Selected Cancer Deaths in Montrose County for Three Times during 1950–2000 for Both Sexes Combined

Cancer (ICD 9)	1950–1969			1970–1984			1985–2000		
	Obs[a]	SMR_{co}	RR[b]	Obs[a]	SMR_{co}	RR[b]	Obs[a]	SMR_{co}	RR[b]
All cancers (140–208)	470	1.03	1.10	508	0.99	1.04	899	0.96	0.94
Esophagus (150)	5	0.94	1.04	6	0.87	1.15	11	0.58	0.51
Stomach (151)	45	1.22	1.23	23	1.18	1.47	19	0.80	0.81
Colon/rectum (153, 154)	55	0.89	1.03	53	0.78	0.81	99	0.94	0.98
Pancreas (157)	33	1.27	1.04	25	0.86	0.88	63	1.21	1.27
Lung (162)	67	1.14	1.28	133	1.22*	1.18	254	1.11	0.98
Skin (172, 173)	16	2.07*	1.96	8	0.83	0.87	13	0.64	0.71
Malignant melanoma of the skin (172)	11	2.49*	1.97	4	0.52	0.50	10	0.64	0.71
Breast (174)	35	0.91	1.08	32	0.71	0.72	59	0.79	0.84
Cervix uteri (180)	9	0.69	0.91	3	0.51	0.63	3	0.49	0.50
Corpus uteri (182)	7	0.86	0.75	10	1.50	2.07	17	1.77*	1.52
Ovary (183)	14	1.05	1.15	14	0.94	0.91	21	0.82	0.85
Prostate (185)	36	1.14	1.04	44	1.26	1.32	68	0.95	0.96
Urinary bladder (188)	12	0.87	1.01	12	0.92	0.92	20	0.93	1.08
Kidney (189)	6	0.63	0.54	9	0.79	0.91	19	0.90	0.86
Liver and kidney (155, 189)	28	1.07	0.89	22	0.89	1.10	38	0.84	0.86
Bone (170)	3	1.06	0.98	LT3	1.14	1.19	3	1.64	2.65
Connective tissue (171)	LT3	0.91	2.16	3	0.97	1.02	7	1.04	1.29
Brain and CNS (191, 192)	4	0.36*	0.41	13	0.95	0.91	27	1.10	1.15
Thyroid (193)	LT3	1.03	0.86	LT3	1.53	1.49	LT3	0.42	0.41
Non-Hodgkin lymphoma (200, 202)	14	0.95	0.89	16	0.92	1.04	45	1.11	1.11
Hodgkin lymphoma (201)	7	1.28	1.70	3	0.94	1.06	5	2.01	2.81
Multiple myeloma (203)	3	0.59	0.73	13	1.48	1.49	17	0.89	0.79
Leukemia (204–208)	21	0.83	0.87	14	0.58*	0.60	30	0.77	0.84
Leukemia, CLL (204.1)	0	0.00	0.00	LT3	0.50	0.53	8	0.93	0.81
Leukemia, not CLL	21	0.85	0.89	12	0.59	0.61	22	0.74	0.88
Childhood leukemia (<20 years)	LT3	0.39	0.30	LT3	0.85	0.89	LT3	0.81	0.89
Childhood cancer (<20 years)	7	0.65	0.57	6	1.06	1.17	LT3	0.56	0.66

Notes. SMRs based on rates in Colorado population. RRs based on comparison counties.
[a] Observed number of cancer deaths in Montrose County. LT3 denotes less than three deaths.
[b] RR is taken as the SMR_{co} in Montrose County divided by the SMR_{co} in the comparison counties.
* $P < 0.05$.

containing dust. Uranium is ubiquitous and is distributed throughout the Earth's crust. Environmental exposures to uranium, however, have not been linked to any detrimental effects (*59*), and the IARC has concluded that there is inadequate evidence to classify uranium as a human carcinogen (*27*). Because uranium has such a long half-life, it is not very radioactive. Chemical toxicity (especially of the kidney) is considered more important for human health than the risk of cancer from uranium's radioactive properties (*59*). Nevertheless, even with respect to chemical toxicity, studies of workers exposed to uranium have failed to demonstrate overt kidney disease (*24, 60*) including end stage renal disease (*7*). Among Montrose County residents, deaths associated with kidney disease were not significantly increased, again suggesting that any environmental exposures to uranium milling products were likely too low to result in toxic effects.

Occupational Studies

Workers exposed to uranium dust during milling, processing and manufacturing have not shown significant or consistent increases in lung cancer, kidney cancer or any other cancer in large-scale occupational studies (*8–10, 27, 61, 62*), so it is not surprising that lower-level environmental exposures are not found to increase cancer risks. One study of uranium processing reported a significant dose response for kidney cancer based on four high-dose cases, but the SMR for kidney cancer was not significantly increased, and the authors concluded that chance was a possible explanation (*63*). Studies of uranium mill workers have reported significant increases of nonmalignant respiratory disease and nonsignificant increases of lymphoma, but the associations were not considered causal because increased risks were not seen among the workers who were employed for the longest time (*7*). Residents of Montrose County were not found to be at significant risk of dying from nonmalignant respiratory disease or from lymphoma.

Radon and Radium

While occupational exposures to high radon levels in underground mines have been shown to increase lung cancer risks, employment in underground mines has not been con-

TABLE 5
Observed (Obs) and Expected (Exp)[a] Numbers of Noncancer Deaths and Standardized Mortality Ratios (SMRs) for Montrose County and the Five Comparison Counties during 1960–1999, and the Estimates of Relative Risk (RR)[b]

Cause of death (ICD 9)	Montrose County				
	Obs[c]	Exp_{US}	Exp_{CO}	SMR_{US}	SMR_{CO}
All causes of death (001–999)	8,617	8,941.7	8,330.3	0.96*	1.03*
Tuberculosis (010–018)	15	12.1	10.7	1.24	1.40
All malignant neoplasms (140–208)	1,610	1,888.0	1,620.1	0.85*	0.99
Diabetes mellitus (250)	152	173.9	139.8	0.87	1.09
Cerebrovascular disease (430–438)	720	755.2	659.2	0.95	1.09*
All heart disease (390–398, 404, 410–429)	2,638	3,316.8	2,705.9	0.80*	0.97
Hypertension with heart disease (402, 404)	58	104.4	71.7	0.56*	0.81
Hypertension without heart disease (401, 403, 405)	23	38.1	35.3	0.60*	0.65*
Non-malignant respiratory disease (460–519)	897	708.5	903.0	1.27*	0.99
Influenza and pneumonia (480–487)	318	300.2	356.7	1.06	0.89
Bronchitis, emphysema, asthma (490–493)	188	133.3	181.3	1.41*	1.04
Bronchitis (490, 491)	37	34.5	43.3	1.07	0.85
Emphysema (492)	126	83.7	116.3	1.51*	1.08
Asthma (493)	25	15.1	21.7	1.65*	1.15
Ulcer of stomach and duodenum (531–533)	44	33.1	39.1	1.33	1.12
Cirrhosis of liver (571)	97	114.7	109.2	0.85	0.89
Nephritis and nephrosis (580–589)	68	69.8	59.7	0.97	1.14
All external causes of death (800–999)	810	572.6	667.8	1.41*	1.21*
Accidents (850–949)	595	399.7	446.7	1.49*	1.33*
Motor vehicle accidents (810–825)	270	186.6	197.9	1.45*	1.36*
All other accidents (800–807, 826–949)	325	213.1	248.8	1.53*	1.31*
Suicides (950–959)	174	115.7	162.6	1.50*	1.07
Homicides and other external causes (960–978, 980–999)	41	57.2	58.5	0.72*	0.70*

[a] Expected numbers based on U.S. rates (Exp_{US}) and on Colorado rates (Exp_{CO}).
[b] RR is taken as the SMR_{CO} for Montrose County divided by the SMR_{CO} for the comparison counties.
[c] The observed numbers were estimated by applying the age, calendar year, sex and cause-specific mortality rates for Montrose County for 1960–1999 to the corresponding Montrose County population data. All cancer deaths were accurately known and comparison with these known values validated the estimation procedure. Slight differences might occur, however, due to rounding.
* $P < 0.05$.

vincingly associated with any other cancer (*23, 25*). Again, were environmental (as opposed to occupational) radon exposure the cause of elevated lung cancer rates observed in males living in Montrose County, a corresponding increase should have been observed in females, but it was not. Risk of leukemia has been investigated in case-control studies of residential radon exposures, but no significant associations were found (*27, 30, 31*). Leukemia and childhood leukemia did not occur at elevated rates among Montrose County residents in the current or previous county mortality studies (*43, 44*).

Vanadium

Carnotite ore also was processed to extract vanadium in addition to uranium and is another source of potential exposure. No human study has linked vanadium to increased cancer rates (*41, 64*), but one animal study recently reported significant elevations of lung cancer in rats, although not mice, after 2 years of continuous inhalation of vanadium pentoxide (*42*). There is some evidence that very large exposures to vanadium could result in kidney damage (*64*). Thus, if vanadium exposures were to result in adverse health effects among residents of Montrose County, they would likely involve damage to the lungs and/or kidney. Similar to the discussion of uranium and radiation exposure, it would be implausible that environmental exposure to vanadium would increase the risk of lung cancer among males while decreasing the risk among females. Further, kidney cancer and kidney disease were not significantly increased among Montrose county residents.

Strengths and Limitations

Strengths of our geographical correlation study include the availability of mortality data that spanned over 50 years, the long history of milling and mining operations in Montrose County from the early 1900s to after 1970, the large number of uranium mines ($n = 223$) and mills ($n = 2$), the availability of several comparison populations, the use of previously accepted methodologies, and the insights provided by previous county, occupational and residential studies of Colorado Plateau populations. Evaluation of both cancer and noncancer mortality is another unique strength of this county investigation.

The minimum latent period for the development of solid cancer after radiation exposure is approximately 5 to 10 years and for leukemia approximately 2 years (*33-35*).

TABLE 5
Extended

Comparison counties						
Obs[a]	Exp_{loc}	Exp_{reg}	SMR_{loc}	SMR_{co}	RR[b]	95% CI
54,125	58,381.1	54,392.5	0.93*	1.00	1.04*	1.02–1.00
51	80.7	71.2	0.63*	0.72*	1.96*	1.10–3.49
10,117	12,004.8	10,315.8	0.84*	0.98	1.01	0.96–1.07
968	1,134.3	910.8	0.85*	1.06	1.02	0.86–1.21
4,600	5,176.4	4,515.5	0.89*	1.02	1.07	0.99–1.16
17,912	21,996.4	18,019.4	0.81*	0.99	0.98	0.94–1.02
557	712.4	495.3	0.78*	1.12*	0.72*	0.55–0.94
240	256.4	238.9	0.94	1.00	0.65*	0.42–0.99
5,548	4,570.2	5,842.4	1.21*	0.95*	1.05	0.97–1.12
2,085	1,990.5	2,386.4	1.05	0.87*	1.02	0.91–1.15
1,128	855.3	1,168.1	1.32*	0.97	1.07	0.92–1.25
262	218.1	273.5	1.20*	0.96	0.89	0.63–1.26
742	540.0	755.1	1.37*	0.98	1.10	0.91–1.33
124	97.2	139.5	1.28*	0.89	1.30	0.84–1.99
242	218.9	261.6	1.11	0.93	1.22	0.88–1.68
540	709.7	676.1	0.76*	0.80*	1.11	0.90–1.38
404	451.1	386.5	0.90*	1.05	1.09	0.84–1.41
5,033	3,662.5	4,249.6	1.37*	1.18*	1.02	0.95–1.10
3,678	2,559.1	2,853.8	1.44*	1.29*	1.03	0.95–1.13
1,866	1,187.7	1,256.2	1.57*	1.49*	0.92	0.81–1.04
1,812	1,371.4	1,597.6	1.32*	1.13*	1.15*	1.02–1.30
1,026	725.5	1,017.8	1.41*	1.01	1.06	0.90–1.25
329	377.8	377.9	0.87*	0.87*	0.80	0.58–1.11

Thus, because uranium and vanadium mining and milling activities in Montrose Country began in the early 1900s, there was ample time for any environmental exposures to accumulate and any effects on resident populations to be detected during 1950–2000. Mortality occurring before 1950 could not be evaluated because county mortality data are not readily available before then.

Comparing the mortality experience of residents of Montrose County with that of demographically similar counties in Colorado followed the methods used by the National Cancer Institute in similar studies (*43, 45*). The use of local comparison populations rather than the state of Colorado or the entire United States minimizes biases possibly associated with different demographic and socioeconomic features that cannot be easily controlled for in analyses. For example, an early report of an excess of chronic renal disease among miners of the Colorado Plateau based on comparisons with U.S. rates was not apparent when comparisons were made based on rates in the corresponding four-state area (*24*). Finally, the Montrose County mortality analyses could be interpreted in light of findings from previous studies; e.g., the excess of lung cancer in men but not women was consistent with an occupational exposure to radon and tobacco use in underground mines previously reported in Uravan and Montrose County (*20, 44*). The excess of tuberculosis and accidental deaths among men but not women was similarly consistent with findings from studies of underground miners of the Colorado Plateau (*24*).

Common to all ecological or geographic correlation studies, however, our study could not assign exposure levels to individuals or directly control for potential confounding factors such as cigarette smoking (*65*). However, because the milling and mining operations in Montrose County began many years before 1950, and because there were many more uranium mines in Montrose County than any other county in Colorado, it is reasonable to assume that the residents of Montrose County experienced more environmental exposures over time than residents of other counties, albeit at presumably low levels. The comparison counties were selected to have similar demographic and socioeconomic characteristics so that personal habits such as use of tobacco products and diet or other potentially confounding factors might be as similar as possible to those of residents of Montrose County. The slightly lower socioeconomic status among Montrose Country residents than the comparison county residents and Colorado state residents suggests that this selection process was not perfect. However, the lower measures of socioeconomic status would act in the direction of increasing the SMRs and RRs in Montrose County, and no consistent increases were seen.

Common to all geographical correlation studies, the comparison counties also could not be perfectly matched on all characteristics. Mesa County, for example, had a higher population density than Montrose County and included some residents who had engaged in uranium mill and mine activities, which might have reduced the magnitude of any

TABLE 6
Standardized Mortality Ratios (SMRs) and Relative Risks (RRs) for Selected Noncancer Deaths in Montrose County for Three Time Periods during 1960–1999 for Both Sexes Combined

Cause of death (ICD 9)	1960–1969			1970–1984			1985–1999		
	Obs[a]	SMR_{co}	RR[b]	Obs[a]	SMR_{co}	RR[b]	Obs[a]	SMR_{co}	RR[b]
All causes of death (001–999)	1,816	1.10*	1.14*	2,817	1.01	1.02	3,984	1.03	1.01
Tuberculosis (010–018)	11	1.89	3.07*	LT3	0.66	0.76	LT3	1.11	1.39
All malignant neoplasms (140–208)	255	1.05	1.12	508	0.99	1.04	846	0.98	0.97
Diabetes mellitus (250)	47	2.24*	1.90*	43	1.01	1.01	62	0.81	0.76*
Cerebrovascular disease (430–438)	215	1.31*	1.22*	265	1.14	1.05	239	0.91	1.00
All heart disease (390–398, 404, 410–429)	599	1.01	1.05	890	0.89*	0.94	1,149	1.03	0.97
Hypertension with heart disease (402, 404)	28	1.05	0.77	17	0.97	0.93	13	0.47*	0.52*
Hypertension without heart disease (401, 403, 405)	8	1.00	1.31	7	0.80	0.76	8	0.43*	0.39*
Non-malignant respiratory disease (460–519)	119	0.83*	0.96	295	1.13	1.24*	483	0.97	0.97
Influenza and pneumonia (480–487)	56	0.67*	0.94	123	1.13	1.39*	130	0.85	0.84
Bronchitis, emphysema, asthma (490–493)	45	1.04	0.95	48	0.88	0.89	95	1.14	1.30*
Bronchitis (490, 491)	9	1.43	1.95	8	0.84	0.95	20	0.73	0.70
Emphysema (492)	28	0.86	0.73	36	0.90	0.87	61	1.40*	1.84*
Asthma (493)	8	1.82	2.00	4	0.81	0.99	13	1.05	1.16
Ulcer of stomach and duodenum (531–533)	18	1.39	1.66	16	1.32	1.21	10	0.71	0.83
Cirrhosis of liver (571)	26	1.17	1.91*	30	0.72	0.94	42	0.92	1.00
Nephritis and nephrosis (580–589)	13	1.52	1.30	27	1.65*	1.52	28	0.81	0.81
All external causes of death (800–999)	205	1.34*	1.20*	290	1.16*	0.92	315	1.19*	1.03
Accidents (850–949)	170	1.50*	1.23*	212	1.27*	0.90	213	1.29*	1.07
Motor vehicle accidents (810–825)	77	1.55*	1.09	104	1.34*	0.83	89	1.27*	0.91
All other accidents (800–807, 826–949)	93	1.45*	1.37*	108	1.21	0.96	124	1.30*	1.22*
Suicides (950–959)	29	0.91	1.16	58	0.99	0.98	87	1.21	1.09
Homicides and other external causes (960–978, 980–999)	5	0.62	0.75	20	0.82	1.08	15	0.58*	0.58*

Notes. SMRs based on rates in the Colorado population. RRs based on comparison counties.

[a] Observed deaths of deaths in Montrose County. See footnote 3 in Table 5 for explanation of estimation procedure. LT3 denotes less than 3.

[b] RR is taken as the SMR_{ex} for Montrose County divided by the SMR_{co} for the comparison counties.

* $P < 0.05$.

observed associations. Analyses excluding Mesa County (and also Yuma and Logan counties) produced similar results as those based on all five comparison counties (Table 7). Comparisons with the general populations of Colorado and the United States also yielded similar results [e.g., based on Colorado rates, significant increases in lung cancer mortality among men (but not women) were seen only among residents of Montrose County and not the residents of the comparison counties]. The advantages of the five-county analyses over the two-county analyses include statistical precision due to larger numbers and likely validity given the closer similarity of essentially all cancer rates with those of the state of Colorado.

While the fact of death within the study counties is known with certainty, length of residence and migration into and from the counties are not known for individuals. There was in general population growth throughout the years, although there may have been some migration out of Montrose County when the uranium industry became less active in the 1980s. Nonetheless, there would have been ample opportunity for any environmental exposures from milling or mining activities to occur and accumulate from the late 1930s to the 1970s in Montrose County so that any increase in mortality from 1950 to about 1984 related to such exposures could have been observed. Further, there was little evidence that Montrose County experienced population changes different from those of the comparison counties over the years 1950 to 2000. The percentage increase in population growth, for example, was essentially the same for each decade over this period [e.g., the population of Montrose County grew from 15,220 in 1950 to 24,423 in 1990 (or 60%), whereas the population growth in the comparison counties was from 94,341 to 159,318 (or 68%)]. Although immigration of "nonexposed" persons might be expected to reduce somewhat the magnitude of the risk associated with possible environmental exposures, much of the increase in Montrose County was related to employment opportunities in the uranium industry and associated occupational and environmental exposures.

Our study is of mortality and not incidence. However, because reporting of deaths is likely to be similar within Montrose County and the comparison counties, and many of the diseases of interest (e.g., lung cancer), have a high fatality rate, mortality would be expected to reflect incidence fairly closely. The current 5-year survival rate for

TABLE 7

Observed (Obs) and Expected (Exp)[a] Numbers of Cancer Deaths and SMRs Occurring in the Two Most Similar Comparison Counties (Delta and Montezuma) during 1950–2000, and the Estimates of Relative Risk (RR)[b] Comparing Montrose County with These Two Counties

	Delta and Montezuma						
Cancer (ICD 9)	Obs	Exp_{us}	Exp_{co}	SMR_{us}	SMR_{co}	RR[b]	95% CI
All cancers (140–208)	3,254	3,981.4	3,467.5	0.82*	0.94*	1.05	0.99–1.11
Esophagus (150)	45	71.3	56.8	0.63*	0.79	0.89	0.53–1.48
Stomach (151)	142	168.6	153.0	0.84*	0.93	1.17	0.89–1.52
Colon/Rectum (153, 154)	384	518.6	435.0	0.74*	0.88*	1.00	0.85–1.19
Pancreas (157)	195	204.6	196.8	0.95	0.99	1.14	0.91–1.43
Lung (162)	710	940.8	713.6	0.75*	0.99	1.15*	1.02–1.29
Skin (172, 173)	79	66.0	65.6	1.20	1.20	0.82	0.55–1.21
Malignant melanoma of the skin (172)	60	45.3	47.3	1.33*	1.27	0.71	0.45–1.13
Breast (174)	240	312.9	284.3	0.77*	0.84*	0.94	0.76–1.17
Cervix uteri (180)	47	48.8	45.9	0.96	1.02	0.58	0.33–1.05
Corpus uteri (182)	60	55.3	45.8	1.08	1.31	1.06	0.70–1.62
Ovary (183)	92	100.9	97.4	0.91	0.94	0.96	0.68–1.36
Prostate (185)	264	255.2	261.7	1.03	1.01	1.06	0.87–1.30
Urinary bladder (188)	61	106.7	90.6	0.57*	0.67*	1.35	0.92–1.99
Kidney (189)	68	80.5	75.7	0.84	0.90	0.90	0.60–1.36
Liver and kidney (155, 189)	178	195.0	176.4	0.91	1.01	0.91	0.70–1.17
Bone (170)	6	14.9	11.2	0.40*	0.54	2.33	0.81–6.73
Connective tissue (171)	10	20.4	21.1	0.49*	0.47*	2.10	0.91–4.87
Brain and CNS (191, 192)	97	88.4	83.8	1.10	1.16	0.77	0.54–1.10
Thyroid (193)	5	10.6	10.5	0.47	0.48	1.86	0.54–6.43
Non-Hodgkin lymphoma (200, 202)	111	135.3	129.4	0.82*	0.86	1.20	0.90–1.61
Hodgkin lymphoma (201)	12	21.9	19.0	0.55*	0.63	2.14	0.99–4.57
Multiple myeloma (203)	75	58.3	60.4	1.29*	1.24	0.81	0.54–1.21
Leukemia (204–208)	133	162.7	158.1	0.82*	0.84	0.87	0.65–1.17
Leukemia, CLL (204.1)[c]	20	24.0	23.9	0.83	0.84	0.91	0.43–1.95
Leukemia, not CLL	111	137.2	133.1	0.81*	0.83	0.88	0.64–1.22
Childhood leukemia (<20 years)	15	13.8	13.5	1.08	1.11	0.51	0.19–1.42
Childhood cancer (<20 years)	24	33.9	31.2	0.71	0.77	0.97	0.51–1.85

[a] Expected numbers based on U.S. rates (Exp_{us}) and on Colorado rates (Exp_{co}).

[b] RR is taken as the SMR_{co} for Montrose County divided by the SMR_{co} for the two comparison counties (see Table 2 for the observed numbers of cancer deaths and SMR_{co} for Montrose County).

[c] CLL denotes chronic lymphocytic leukemia.

* $P < 0.05$.

lung cancer is 17% (66), whereas in years past, survival was much worse; e.g., in 1960–1973, the median survival time was only 5.4 months (67). Diseases that have a low fatality rate can also be evaluated, although the statistical power to identify an effect would be lower than for an incidence survey because of the smaller number of events. Improvement in treatment would also be expected to be similar between Montrose and the comparison counties so that it is unlikely that study findings would reflect differences in medical care over time. Cancer incidence data exist for Colorado for recent years, 1990–2002. Similar to the patterns for cancer mortality, there were essentially no differences in cancer incidence rates for all cancers over this 13-year period among the residents of Montrose County, the five comparison counties, and the State of Colorado (Fig. 2). Comparable findings are seen for childhood leukemia in that cancer incidence between 1990 and 2002 gave a similar picture as the mortality data [i.e., the rate of leukemia (2.6 per 100,000) was lower than the state of Colorado (4.0 per 100,000) and the difference was not statistically significant].

Finally, the entire county rather than smaller areas in the immediate vicinity of specific mining or milling facilities was used as the geographic unit for analysis. This was necessitated because mortality data extending back to 1950 are available only at the county level. However, mining and milling facilities were widespread throughout large parts of western Montrose County so that the potential for environmental exposure was not limited to any single area. There were 223 uranium mines and two uranium mills in Montrose County, and the average density of about one uranium facility per 10 square miles was much greater than that for the state of Colorado or the comparison counties. Further, a comprehensive cohort study of residents of the town of Uravan from 1937 and followed through May 1984 reached similar conclusions based on both cancer incidence and mortality data (i.e., there was no significant increase in any cancer or disease except lung cancer among men attributed

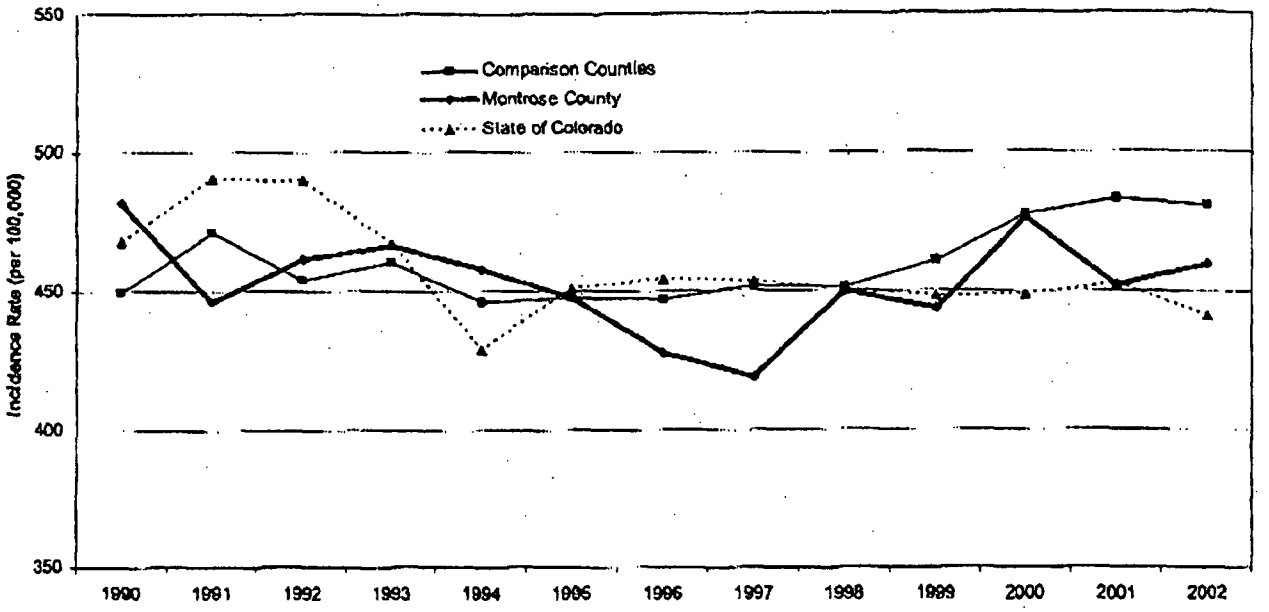

FIG. 2. Age-adjusted cancer incidence rates for all cancers in Montrose County, the five comparison counties, and the state of Colorado from 1990–2002. Except for the first 2 calendar years, 3-year moving averages are presented to smooth fluctuations in rates due to relatively small numbers of cancer cases occurring in a single year for Montrose County and the five comparison counties. Source: Colorado Department of Public Health and Environment (http://www.cdphe.state.co.us/cohid/agreement.html).

to documented employment in underground mines and tobacco use (*20*)].

Summary

In summary, there is no evidence that residents of Montrose County experienced an increased risk of dying of cancer or other diseases because of environmental exposures associated with uranium and vanadium milling and mining activities. Although descriptive correlation analyses such as this preclude definitive causal inferences on their own, an occupational risk of lung cancer due to underground mining exposure to radon and smoking is suggested among males and consistent with previous cohort studies of underground miners of the Colorado Plateau and of residents of a milling and mining community in Montrose County.

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Appendix 7

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A cohort study of uranium millers and miners of Grants, New Mexico, 1979–2005

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Abstract

A cohort mortality study of workers engaged in uranium milling and mining activities near Grants, New Mexico, during the period from 1955 to 1990 was conducted. Vital status was determined through 2005 and standardised mortality ratio (SMR) analyses were conducted for 2745 men and women alive after 1978 who were employed for at least six months. Overall, mortality from all causes (SMR 1.15; 95% CI 1.07–1.23; $n = 818$) and all cancers (SMR 1.22; 95% CI 1.07–1.38; $n = 246$) was greater than expected on the basis of US mortality rates. Increased mortality, however, was seen only among the 1735 underground uranium miners and was due to malignant (SMR 2.17; 95% CI 1.75–2.65; $n = 95$) and non-malignant (SMR 1.64; 95% CI 1.23–2.13; $n = 55$) respiratory diseases, cirrhosis of the liver (SMR 1.79; $n = 18$) and external causes (SMR 1.65; $n = 58$). The lung cancer excess likely is attributable to the historically high levels of radon in uranium mines of the Colorado Plateau, combined with the heavy use of tobacco products. No statistically significant elevation in any cause of death was seen among the 904 non-miners employed at the Grants uranium mill. Among 718 mill workers with the greatest potential for exposure to uranium ore, no statistically significant increase in any cause of death of *a priori* interest was seen, i.e., cancers of the lung, kidney, liver, or bone, lymphoma, non-malignant respiratory disease, renal disease or liver disease. Although the population studied was relatively small, the follow-up was long (up to 50 yrs) and complete. In contrast to miners exposed to radon and radon decay products, for uranium mill workers exposed to uranium dusts and mill products there was no clear evidence of uranium-related disease.

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Abbreviations

CI	Confidence interval
ICD-9	Ninth revision of the international classification of diseases
NDI	National death index
NIOSH	National Institute of Occupational Health and Safety
SMR	Standardised mortality ratio
SSA	Social security administration

1. Introduction

Underground uranium miners exposed to high levels of radon and radon decay products are at increased risk of lung cancer but apparently no other cancer (Wagoner *et al* 1965, Lundin *et al* 1971, Whittemore and McMillan 1983, Hornung and Meinhardt 1987, Samet *et al* 1991, Lubin *et al* 1995, Darby *et al* 1996, NRC 1999). Several non-cancer causes of death (i.e., tuberculosis, non-malignant respiratory disease and accidents), however, were increased among early miners in the United States (Archer *et al* 1976, Roscoe 1997).

Uranium mill workers, however, have not been consistently found to be at increased risk for cancer. The National Institute for Occupational Health and Safety (NIOSH) conducted a study of 1484 men who worked at one of seven uranium mills on or after January 1, 1940 and reported a statistically significant increase in non-malignant respiratory disease mortality (SMR 1.43; $n = 100$) and non-statistically significant increases in mortality from lung cancer, lymphoma, and kidney disease (Pinkerton *et al* 2004). The authors were cautious in interpreting their findings, however, because increased length of employment (and assumed increased exposure to uranium compounds) was not associated with increased mortality from any of these conditions. A recent study of 450 uranium mill workers at Uravan, Colorado followed through 2004 revealed no statistically significant excess deaths from any cause, including non-malignant respiratory disease (SMR 0.99; $n = 24$) and lung cancer (SMR 1.26; $n = 24$) (Boice *et al* 2007b). Some of the uranium millers in the Uravan study were also included in the NIOSH study.

Although there have been many studies of underground uranium miners, few studies have been conducted of uranium millers. Exposures among these two groups differ appreciably, with underground miners being exposed primarily to radon and radon decay products, and millers being exposed primarily to uranium ore dust and mill products but not radon. Other than the recent study of Uravan uranium workers, there have been few studies of a workforce that includes both miners and millers. We report here such a study of workers employed by a large milling and mining company in Grants, New Mexico.

1.1. Exposure potential

The Grants, New Mexico uranium belt is an area of 100 by 25 miles in Cibola, McKinley and Sandoval Counties. In the 1950s and 1960s, 60 mines and five mills were in operation and New Mexico led the nation in uranium production (Samet *et al* 1983). The chief mining districts were Laguna, Ambrosia Lake and Church Rock.

The heyday of New Mexico mining and milling activities began in the mid to late 1950s and after the hazards of underground mining had been recognised in studies by the US Public Health Service (Lundin *et al* 1971). As such, state and federal regulations limited radon progeny exposures and New Mexico miners experienced generally lower cumulative exposures than for

other miners of the Colorado plateau (Morgan and Samet 1986). Nonetheless, a statistically significant risk of lung cancer (SMR 4.0; $n = 68$) was reported among 3469 male miners from New Mexico with a mean cumulative exposure concentration of 111 WLM (Samet *et al* 1991). An increase in external causes of death (SMR 1.5; $n = 173$) was also statistically significant. The mortality data also supported an association between pneumoconiosis and exposure to silica and other dusts (Samet *et al* 1984b, 1991). Increased mortality due to lung cancer, tuberculosis and non-malignant respiratory disease has also been reported among Navajo miners from New Mexico (Wagoner *et al* 1975, Samet *et al* 1984a, Roscoe *et al* 1995)

The Grants uranium mill was located in Cibola County, New Mexico, about 5.5 miles northwest of the Village of Milan and about seven miles northeast of the Town of Grants. Uranium milling began in 1958 and continued through 1990. Radon and radon decay product exposures are relatively insignificant among mill workers due to the aboveground nature of their work. However, there is the potential for exposure to other radioactive substances such as uranium-238, uranium-234 and thorium-230, as well as exposure from uranium ore dust, vanadium pentoxide, yellowcake, ammonium diuranate, silica and slight traces of radium-226 (Waxweiler *et al* 1983).

Uranium milling involves ore crushing and grinding; ore leaching, i.e., removing and dissolving uranium; uranium recovery from leach solutions; and drying and packaging of yellowcake (uranium oxide, U_3O_8)—the final product of the milling process. Crushing and grinding of ore and yellowcake drying and packaging are dusty operations where inhalation potential is highest. The solid and liquid wastes remaining after uranium is extracted from ore are called tailings, and contain the same radionuclides found in the ore, i.e., uranium, thorium, radium and other decay products. Potential sources of environmental exposures around uranium milling operations include these tailings piles, in addition to runoff collection ponds, ore transport and airborne and liquid effluents (NCRP 1993). There are two tailings piles covering about 200 acres near the Grants uranium mill (EPA 2007).

Radium, a component of mill tailings, occurs naturally in uranium ore but generally is not extracted during the milling process. Ingestion of large amounts of radium by dial painters during the early part of the last century resulted in excesses of bone cancer and a rare carcinoma of the paranasal sinuses, but no other cancer was significantly increased (Fry 1998, IARC 2001). Radium decays into radon gas, a known cause of lung cancer, and also emits gamma radiation, which at sufficiently high levels can cause leukaemia, breast cancer and other malignancies (UNSCEAR 2000, NRC 2006). Leukaemia, however, has not been found to be significantly increased in studies of uranium processors, millers or miners (Harley *et al* 1999, IOM 2001, Pinkerton *et al* 2004, Darby *et al* 1996, NRC 1999, Boice *et al* 2007b, Canu *et al* 2008). Descriptive studies of communities living near uranium milling or processing facilities in Texas (Boice *et al* 2003a), Pennsylvania (Boice *et al* 2003b, 2003c) and Colorado (Boice *et al* 2007a) also provide little evidence for elevated rates of leukaemia or other cancers associated with penetrating external radiation.

The route of intake and the biological solubility of a given uranium compound influences the potential for chemical or radiological toxicity (ATSDR 1999, IOM 2001). Natural uranium, i.e., uranium ore, is largely soluble and passes through the body rather quickly whether inhaled or ingested (Harley *et al* 1999, Priest 2001). Yellowcake and other mill products are largely insoluble uranium oxides that, if inhaled, would accumulate in the lung and tracheobronchial lymph nodes (ATSDR 1999, Pinkerton *et al* 2004); the tracheobronchial lymph nodes, however, do not appear radiosensitive and are not considered a target for uranium toxicity (Eidson 1994). Different uranium ore processing schemes involve different uranium compounds with different dissolution rates so that workers could be exposed to mixtures of both soluble and insoluble forms of uranium (Eidson and Mewhinney 1980, Eidson 1994). Chemical toxicity, primarily

renal dysfunction, may be a consequence of high intakes of soluble uranium. Lung injury may occur after high intakes of insoluble uranium. In general, ingested uranium is poorly absorbed from the intestinal tract and retention in the body would be low (ATSDR 1999, IOM 2001).

Based on associations reported in previous studies of uranium millers and miners and knowledge of the likely distribution of uranium within body tissues after inhalation or ingestion (Leggett 1989, ATSDR 1999, IARC 2001), we focused our attention on cancers of the lung, kidney, liver and bone, lymphoma and non-malignant respiratory, non-malignant renal and non-malignant liver diseases.

2. Material and methods

A retrospective cohort mortality study was conducted of uranium miners and millers of Grants, New Mexico. Institutional Review Board approval of the research protocol was received from Independent Review Consulting, Inc. (www.irb-irc.com).

2.1. Population identification

All uranium miners and millers who worked for a large uranium mining and milling company in Grants, New Mexico were eligible for study. The study population was identified from computerised listings of 3390 company personnel (1955–1991) and from overlapping job history records for 5606 workers (1955–2001). Duplicates were removed and persons without identifying information excluded (figure 1). We also excluded persons who worked less than 6 months.

2.1.1. Demographic information. Available demographic information included name, date of birth, social security number, sex, marital status and current address.

2.1.2. Work histories. Available work history information included year of hire, year of termination, pay type (hourly, salaried) and job history (job location, department, job title). Employment at uranium mines and mills was readily determined on the basis of job location (mine or mill) and job title (e.g., miner, underground labourer, driller, shaftman, tailings pile operator, yellowcake filter and dryer operator, crusher operator). Everyone who worked underground was classified as a 'miner' regardless of job classification. A sample of 19 millers was submitted to NIOSH to learn of any additional uranium work that was not known from the existing company records. Similarly, linkages of worker rosters were made with a Colorado milling and mining study (Boice *et al* 2007b). NIOSH had conducted health studies of uranium millers (Pinkerton *et al* 2004) and Colorado plateau uranium miners (Roscoe 1997). The NIOSH records often included detailed occupational histories, questionnaires with smoking information, and pathology evaluations for many of the workers. The Grants uranium mill was not one of the seven mills included in the NIOSH study (Pinkerton *et al* 2004), but some of the Grants underground miners were likely included in previous studies of miners in New Mexico (Samet *et al* 1991).

2.1.3. Exposure to ore or uranium processing. Workers who had not worked as an underground miner were classified as to the likelihood that they worked with uranium ore or with the processing of uranium ore at the mill. The assignment of exposure potential was based on job titles (e.g., accountants and clerks were assumed to be unlikely or infrequently exposed to ore or uranium processing activities, whereas crusher operators, yellowcake filter and dryer

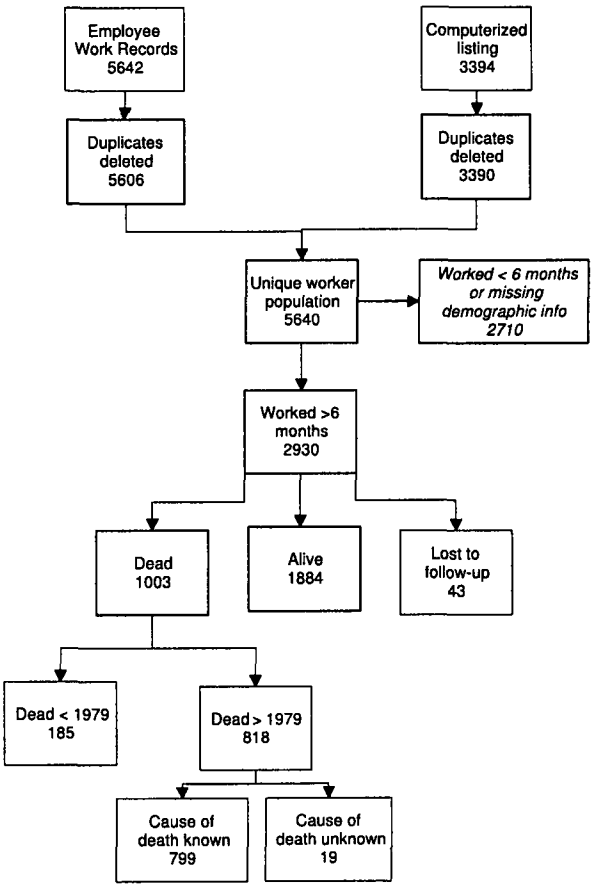

Figure 1. Identification of workers engaged in uranium milling and mining activities near Grants, New Mexico, and vital status as of December 31, 2005. Eligible subjects worked for 6 or more months with sufficient identifying information for tracing; duplicates were removed. Study subjects were assumed alive if NDI and Social Security Administration linkages failed to provide a death or vital status match ($n = 43$).

operators and tailings pond operators were assumed to have had the potential for exposure to ore and uranium dust). Interviews with employees were helpful in resolving uncertainties in specific job titles and work responsibilities. Some employees also lived in Milan and in areas close to the uranium mill.

2.1.4. Length of employment. Persons were categorised as to their length of employment as follows: <6 months (excluded); 6 months to 1.9 yrs; 2–4.9 yrs; ⩾5 yrs. Based on the sample of records submitted to NIOSH, it was learnt that some workers had also been employed at different facilities in other parts of the country. Unfortunately our records of such employment were incomplete and we were unable to incorporate subsequent work histories into the analyses.

2.2. *Follow-up*

Mortality and vital status were determined from various linkages of the study roster with national databases including the National death index (NDI), the Social security administration (SSA) Death Master File and other SSA files, credit bureaus and Comserv, a computer services firm specialising in locating persons. SSA files confirmed that 1750 persons were alive in 2004. Searches with credit bureau records and LexisNexis, an online information service provider (www.lexisnexis.com), confirmed that 177 of the 220 persons without an SSA or NDI match were alive sometime after 1979. The remaining 43 persons (1.5%) without a SSA or NDI mortality match were assumed to be alive. Of the 818 deaths occurring after 1978, cause of death was not obtained for 19 (2.3%) including one person who died outside the United States. Deaths prior to 1979 ($n = 185$) were excluded from the SMR analyses (figure 1, table 1) because cause of death information from the National Death Index is not available before 1979 and attempts to obtain death certificates for these early deaths were in large part unsuccessful. Of the 185 deaths occurring before 1978, death certificates were sought but not obtained for 80 (43.2%) which precluded a meaningful cause of death analysis.

2.3. *Analysis*

Person-years of follow-up began on January 1, 1979 or the date of first employment (plus 6 months), whichever came later (except for those first employed July 1, 1978 to December 31, 1978 for whom follow-up began 6 months after hire date). Follow-up ended on the date of death, December 31, 2005 or age 95, whichever came earlier. There were 6 persons who were withdrawn from follow-up once they reached the age of 95. Standardised mortality ratios (SMR) were computed as the ratio of the observed numbers of deaths to the number of deaths that would have been expected using the mortality rates of the general population of the United States. Observed numbers of deaths from cancers and all other diseases were categorised by sex, age and calendar year for all workers and for subgroups defined by duration of employment and work experience at a uranium mine or uranium mill. Expected numbers of deaths were computed based on age-, calendar year and sex-specific rates in the general population of the United States. SMR analyses based on mortality rates of the general population of New Mexico were also conducted using race weightings of 90% white and 10% non-white. White rates included Hispanics and non-Hispanic whites, and non-white rates included primarily Navajo and other Native Americans. There were very few black workers. SMRs and 95% confidence intervals (95% CI) were calculated using OCMAP software for 41 causes of death categories (Marsh *et al* 1998).

3. Results

Computerised company records and imaged work history records were used to identify 2930 workers (2682 men and 248 women) who worked at least 6 months between 1955 and 2004 (table 1). The average length of time between the date of first employment and the date when follow-up was completed was 36.4 years. Over 28% of the workers had been employed for 5 or more years, and 38% of the workers were followed for more than 40 years after first employment. Just over one-third (34.2%) of the workers were found to have died, 64% were confirmed to be alive at the end of follow-up (December 31, 2005) and 1.5% were assumed to be alive.

After excluding 185 persons who died before 1979, 2745 workers remained for inclusion in the SMR analyses. Nearly 45% of the 818 deaths observed between 1979 and 2005 occurred

Table 1. Demographic and occupational characteristics of uranium millers and miners, Grants, New Mexico, 1955–2005.

	Miners (N = 1867)		Millers[a] (N = 759)		Other/Unk (N = 304)		Total (N = 2930)	
Characteristic	N	%	N	%	N	%	N	%
Gender								
Male	1813	97.1	692	91.2	177	58.2	2682	91.5
Female	54	2.9	67	8.8	127	41.8	248	8.5
Marital status								
Married	820	43.9	304	40.1	144	47.4	1268	43.3
Single	521	27.9	315	41.5	102	33.6	938	32.0
Unknown	306	16.4	133	17.5	51	16.8	490	16.7
Missing	220	11.8	7	0.9	7	2.3	234	8.0
Pay type								
Hourly	1168	62.6	366	48.2	82	27.0	1616	55.2
Salary	521	27.9	315	41.5	102	33.6	938	32.0
Unknown	178	9.5	78	10.3	120	39.5	376	12.8
Year of birth								
<1900	2	0.1	9	1.2	2	0.7	13	0.4
1900–1919	142	7.6	95	12.5	27	8.9	264	9.0
1920–1929	323	17.3	94	12.4	38	12.5	455	15.5
1930–1939	440	23.6	205	27.0	74	24.3	719	24.5
1940–1949	517	27.7	190	25.0	95	31.3	802	27.4
1950–1959	420	22.5	151	19.9	65	21.4	636	21.7
⩾1960	23	1.2	15	2.0	3	1.0	41	1.4
Calendar year of first employment								
1955–1964	603	32.3	339	44.7	99	32.6	1041	35.5
1965–1974	518	27.8	185	24.4	75	24.7	778	26.6
1975–1984	720	38.6	187	24.6	124	40.8	1031	35.2
1985–1989	26	1.4	48	6.3	6	2.0	80	2.7
Years since first employed								
<20	26	1.4	48	6.3	6	2.0	80	2.7
20–29	659	35.3	175	23.1	115	37.8	949	32.4
30–39	543	29.1	175	23.1	75	24.7	793	27.1
40–49	639	34.2	361	47.6	108	35.5	1108	37.8
Year of termination								
Prior to 1960	71	3.8	40	5.3	7	2.3	118	4.0
1960–1969	585	31.3	255	33.6	91	29.9	931	31.8
1970–1979	657	35.2	224	29.5	86	28.3	967	33.0
1980–1989	521	7.9	193	25.4	100	32.9	814	27.8
1990–2004	33	1.8	47	6.2	20	6.6	100	3.4
Duration of employment								
6 months–1.9 yrs	872	46.7	315	41.5	126	41.5	1313	44.8
2–4.9 yrs	489	26.2	216	28.5	73	24.0	778	26.6
5–9.9 yrs	287	15.4	111	14.6	53	17.4	451	15.4
⩾10 yrs	219	11.7	117	15.4	52	17.1	388	13.2
Work with ore or uranium processing[b]								
Likely	0	0.0	759	100	0	0.0	759	25.9
Unlikely	0	0.0	0	0.0	194	63.8	194	6.6
Missing/Not applicable[c]	1867	100.0	0	0.0	110	36.2	1977	67.5

Table 1. (Continued.)

Characteristic	Miners (N = 1867)		Millers[a] (N = 759)		Other/Unk (N = 304)		Total (N = 2930)	
	N	%	*N*	%	*N*	%	*N*	%
Vital status as of 12/31/2005								
Alive (confirmed)	1165	62.4	490	64.6	229	75.3	1884	64.3
Alive (assumed)	25	1.3	8	1.1	6	2.0	43	1.5
Dead after 1978	541	29.0	220	29.0	57	18.8	818	27.9
Dead before 1979	132	7.1	41	5.4	12	4.0	185	6.3

[a] Mill workers with job titles associated with uranium ore or processing activities (e.g., yellowcake dryer).
[b] Tabulations are only for the 953 workers at the Grants mill not known to have worked at a mine.
[c] Miners were not classified as to whether they worked at a uranium mill.

in New Mexico with over 55% occurring in 38 other states, indicating the appropriateness of using US mortality rates for the SMR analyses.

Most of the workers were male (92%) and paid hourly wages (55%), 50% were born before 1940 (average 1938), 62% were hired before 1975 (average 1969) and 69% terminated their employment before 1980 (average 1973) (table 1). There were 1867 (or 64%) workers known to have worked at a uranium mine at some time during their career. There were 1063 workers employed at the uranium mill or proximal facilities with no known mining experience; personnel job history records indicated that 759 of these workers held jobs that were likely to have involved working directly with uranium ore or with uranium processing activities (e.g., yellowcake drying).

Information requested from NIOSH to learn of subsequent employment at other uranium mines and mills was found for 8 (42%) of the 19 mill workers; 3 of the 11 workers without information had been hired after the NIOSH studies had been initiated in 1970. Of the 8 mill workers, one had worked at another uranium mill in Arizona, two as surface workers at uranium mines and two as underground miners. Three had also worked at a mine but details were not available. Linkages of worker rosters had also revealed that 9 of the 904 mill workers had been employed at the Uravan mill in Colorado (Boice *et al* 2007b).

Table 2 presents the observed and expected number of deaths and SMRs for the 2745 workers at uranium mines or mills who were alive in 1979 and followed through 2005 by sex. There were 63 395 person-years of observation (average 23.1 yrs). Overall, 818 workers were found to have died compared with 713.7 expected (SMR 1.15; 95% CI 1.07–1.23). Statistically significant increased numbers of deaths were found for lung cancer (SMR 1.65; 95% CI 1.36–1.97; n = 117), diseases of the nervous system (SMR 1.60; 95% CI 1.01–2.39; n = 23), non-malignant respiratory disease (SMR 1.42; 95% CI 1.14–1.76; n = 84), accidents (SMR 1.44; 95% CI 1.05–1.92; n = 46) and suicides (SMR 1.61; 95% CI 1.04–2.37; n = 25). The only cause with statistically significant decreased numbers of deaths was AIDS (SMR 0.0; expected number 7.2). Lung cancer was increased only among males. There were no statistically significant findings among the small number of 245 female workers.

The observed numbers of deaths were not statistically different from the expected numbers in the general population for cancers of the kidney (SMR 1.11; 95% CI 0.41–2.42; n = 6) and liver (SMR 1.70; 95% CI 0.78–3.23; n = 9) or for non-Hodgkin lymphoma (SMR 0.75; 95% CI 0.28–1.64; n = 6), leukaemia other than CLL (SMR 1.36; 95% CI 0.59–2.68; n = 8), heart disease (SMR 0.93; 95% CI 0.81–1.06; n = 218), liver cirrhosis (SMR 1.47; 95% CI 0.93–2.21; n = 23) or non-malignant kidney disease (SMR 0.86; 95% CI 0.32–1.87; n = 6).

Table 2. Observed and expected numbers of deaths and standardised mortality ratios (SMRs) among employees at uranium mills or mines near Grants, New Mexico, followed 1979–2005, by sex.

Sex	Males				Females				Total			
No. of persons	2500				245				2745			
Person-years	57 284				6110				63 395			
Cause of death (ICD9)	Obs	Exp	SMR	95% CI	Obs	Exp	SMR	95% CI	Obs	Exp	SMR	95% CI
All causes of death (001–999)	789	689.3	1.15[b]	1.07–1.23	29	24.4	1.19	0.80–1.70	818	713.7	1.15[b]	1.07–1.23
All malignant neoplasms (140–208)	235	192.2	1.22[b]	1.07–1.39	11	9.3	1.18	0.59–2.11	246	201.5	1.22[b]	1.07–1.38
Buccal cavity and pharynx (140–149)	1	4.1	0.25	0.01–1.37	1	0.1	10.9	0.27–60.8	2	4.2	0.48	0.06–1.73
Oesophagus (150)	4	6.0	0.67	0.18–1.71	0	0.1	0.00	—	4	6.1	0.66	0.18–1.69
Stomach (151)	5	5.1	0.99	0.32–2.30	0	0.1	0.00	—	5	5.2	0.96	0.31–2.24
Colon (153)	11	15.9	0.69	0.35–1.24	0	0.6	0.00	—	11	16.5	0.67	0.33–1.19
Rectum (154)	1	3.1	0.33	0.01–1.82	0	0.1	0.00	—	1	3.2	0.32	0.01–1.76
Biliary passages and liver (155, 156)	9	5.1	1.76	0.80–3.34	0	0.2	0.00	—	9	5.3	1.70	0.78–3.23
Pancreas (157)	7	9.6	0.73	0.29–1.50	2	0.4	5.01	0.61–18.1	9	10.0	0.90	0.41–1.71
Bronchus, trachea, and lung (162)	114	68.8	1.66[b]	1.37–1.99	3	2.4	1.27	0.26–3.72	117	71.1	1.65[b]	1.36–1.97
Breast (174, 175)	0	0.2	0.00	0.00–15.9	2	2.0	1.00	0.12–3.62	2	2.2	0.90	0.11–3.25
All uterine (179–182)	—	—	—	—	0	0.4	0.00	0.00–8.35	0	0.4	0.00	0.00–8.35
Other female genital organs (183–184)	—	—	—	—	2	0.6	3.17	0.38–11.5	2	0.6	3.17	0.38–11.5
Prostate (185)	13	14.6	0.89	0.47–1.52	—	—	—	—	13	14.6	0.89	0.47–1.52
Kidney (189.0–189.2)	6	5.3	1.14	0.42–2.49	0	0.2	0.00	0.00–24.3	6	5.4	1.11	0.41–2.42
Bladder and other urinary (188, 189.3–189.9)	3	4.9	0.61	0.13–1.80	1	0.1	13.1	0.33–72.7	4	5.0	0.81	0.22–2.07
Melanoma of skin (172)	6	3.7	1.63	0.60–3.54	0	0.1	0.00	—	6	3.8	1.57	0.57–3.41
Brain and CNS (191–192)	5	5.4	0.93	0.30–2.16	0	0.3	0.00	—	5	5.7	0.88	0.29–2.06
Thyroid and other endocrine glands (193–194)	1	0.6	1.82	0.05–10.1	0	0.0	0.00	—	1	0.6	1.71	0.04–9.52
Bone (170)	0	0.4	0.00	0.00–10.3	0	0.0	0.00	—	0	0.4	0.00	0.00–9.87
All lymphatic, haematopoietic tissue (200–208)	23	18.8	1.22	0.78–1.84	0	0.8	0.00	0.00–4.87	23	19.6	1.18	0.75–1.77
Non-Hodgkin lymphoma (200, 202)	6	7.6	0.79	0.29–1.71	0	0.3	0.00	—	6	8.0	0.75	0.28–1.64
Hodgkin lymphoma (201)	1	0.7	1.52	0.04–8.48	0	0.0	0.00	—	1	0.7	1.45	0.04–8.08
Leukaemia and aleukaemia (204–208)	12	7.1	1.69	0.87–2.95	0	0.3	0.00	—	12	7.4	1.62	0.84–2.83

Table 2. (Continued.)

Sex	Males				Females				Total			
No. of persons	2500				245				2745			
Person-years	57284				6110				63395			
Cause of death (ICD9)	Obs	Exp	SMR	95% CI	Obs	Exp	SMR	95% CI	Obs	Exp	SMR	95% CI
Chronic lymphocytic leukaemia (204.1)	4	1.5	2.71	0.74–6.93	0	0.0	0.00	—	4	1.5	2.65	0.72–6.79
Leukaemia other than CLL	8	5.6	1.42	0.61–2.80	0	0.2	0.00	—	8	5.9	1.36	0.59–2.68
Multiple myeloma (203)	4	3.2	1.24	0.34–3.16	0	0.1	0.00	—	4	3.4	1.19	0.32–3.04
Pleura and peritoneum (158.8, 158.9, 163) and mesothelioma (ICD10 C45)[a]	2	0.7	2.71	0.33–9.80	0	0.0	0.00	—	2	0.8	2.66	0.32–9.61
AIDS (042–044, 795.8)	0	7.1	0.00[b]	0.00–0.52	0	0.1	0.00	—	0	7.2	0.00[b]	0.00–0.51
Diabetes (250)	19	15.9	1.20	0.72–1.87	1	0.8	1.31	0.03–7.29	20	16.6	1.20	0.74–1.86
Mental and behavioural disorders (290–319)	9	8.0	1.13	0.52–2.14	0	0.2	0.00	—	9	8.2	1.10	0.50–2.08
Diseases of the nervous system (320–389)	21	13.8	1.52	0.94–2.32	2	0.6	3.29	0.40–11.9	23	14.4	1.60[b]	1.01–2.39
Cerebrovascular disease (430–438)	30	31.4	0.95	0.64–1.36	2	1.2	1.61	0.20–5.81	32	32.7	0.98	0.67–1.38
All heart disease (390–398, 404, 410–429)	212	228.9	0.93	0.81–1.06	6	5.2	1.16	0.43–2.53	218	234.0	0.93	0.81–1.06
Non-malignant respiratory disease (460–519)	83	57.1	1.45[b]	1.16–1.80	1	1.9	0.52	0.01–2.91	84	59.1	1.42[b]	1.14–1.76
Bronchitis, emphysema, asthma (490–493)	35	18.8	1.86[b]	1.30–2.59	0	0.9	0.00	0.00–4.28	35	19.7	1.78[b]	1.24–2.48
Cirrhosis of liver (571)	22	15.1	1.46	0.91–2.20	1	0.5	2.02	0.05–11.3	23	15.6	1.47	0.93–2.21
Nephritis and nephrosis (580–589)	6	6.7	0.89	0.33–1.94	0	0.2	0.00	0.00–15.1	6	7.0	0.86	0.32–1.87
All external causes of death (800–999)	77	52.1	1.48[b]	1.17–1.85	1	1.8	0.56	0.01–3.10	78	53.9	1.45[b]	1.14–1.81
Accidents (850-949)	46	30.9	1.49[b]	1.09–1.99	0	1.1	0.00	0.00–3.40	46	32.0	1.44[b]	1.05–1.92
Suicides (950-959)	24	15.1	1.59[b]	1.02–2.37	1	0.5	2.20	0.06–12.3	25	15.5	1.61[b]	1.04–2.37
Unknown causes of death	18				1				19			

[a] Mesothelioma was not a codeable cause of death until 1999; ICD10 (C45). Before 1999, cancers of the pleura and peritoneum (ICD9 158.8, 158.9, 163) have been used to approximate mesothelioma mortality.
[b] $p < 0.05$.

No deaths were observed for bone cancer (0.4 expected) and only one death occurred from cancer of the thyroid (0.6 expected).

Table 3 presents the observed and expected number of deaths and SMRs by employment at a uranium mine. Among the 1735 miners, the total number of deaths, 541, was statistically higher than expected, 426.4 (SMR 1.27; 95% CI 1.16–1.38). The excess number of deaths among workers with mining experience arose primarily from five causes: lung cancer (SMR 2.17; 95% CI 1.75–2.65; $n = 95$); non-malignant respiratory diseases (i.e., bronchitis, emphysema and asthma combined, influenza and pneumonia) (SMR 1.64; 95% CI 1.23–2.13; $n = 55$), cirrhosis of the liver (SMR 1.79; 95% CI 1.06–2.83; $n = 18$), accidents (SMR 1.50; 95% CI 1.02–2.13; $n = 31$) and suicides (SMR 2.06; 95% CI 1.28–3.15; $n = 21$). Among men with mining experience, heart disease occurred as expected (SMR 0.96; 95% CI 0.80–1.14; $n = 133$).

The overall SMR for the 106 workers whose mining experience was unknown was 0.95 (95% CI 0.61–1.42; $n = 24$) and their total-cancer SMR was 0.58 (95% CI 0.16–1.47; $n = 4$).

There were no statistically significant high or low SMRs among the 904 workers not known to have worked at a uranium mine. Their overall SMR for all causes of death was 0.97 (95% CI 0.85–1.09) and their total-cancer SMR was 0.89 (95% CI 0.69–1.14). Lung cancer was not increased (SMR 0.85; 95% CI 0.52–1.29; $n = 21$), nor was non-malignant respiratory disease (SMR 1.07; 95% CI 0.69–1.58; $n = 25$). Deaths from heart disease occurred below expectation (SMR 0.84; 95% CI 0.66–1.05; $n = 73$).

Table 4 presents the observed and expected numbers of deaths and SMRs for the 904 workers at the uranium mill who were not known to have worked at a mine. Among the 718 millers with the highest potential for exposure to uranium ore, there were no statistically significant increased causes of death. The all-cause SMR was 1.00 (95% CI 0.87–1.14; $n = 220$), the total-cancer SMR was 0.94 (95% CI 0.71–1.22; $n = 56$), the lung cancer SMR was 0.88 (95% CI 0.52–1.38; $n = 18$), the SMR for non-malignant respiratory disease was 1.22 (95% CI 0.78–1.81; $n = 24$), the SMR for non-malignant kidney disease was 1.30 (95% CI 0.27–3.79; $n = 3$) and the SMR for heart disease was 0.84 (95% CI 0.65–1.08; $n = 63$).

SMR analyses were conducted for uranium millers not known to have worked at an underground mine by duration of employment (data not shown). There were no statistically significant increased SMRs for any cause of death for those employed for the longest time. The all-cause SMR for the 209 persons who worked for more than 5 yrs (SMR 0.87; 95% CI 0.70–1.07; $n = 88$) was slightly lower than for all 718 mill workers combined (SMR 1.00), as were the SMRs for total cancer (0.72; $n = 19$), lung cancer (0.56; $n = 5$) and non-malignant respiratory disease (0.68; $n = 7$), although the numbers were small. A decreased risk of heart disease (SMR 0.77; 95% 0.51–1.11; $n = 28$) was consistent with the low SMR (0.84) seen for all millers.

SMR analyses were conducted using general population rates for the state of New Mexico and the mortality patterns were generally similar to those using rates for the United States. The all-cause SMR among all workers was 1.19 (95% CI 1.11–1.28) and similar to the SMR of 1.15 (95% CI 1.07–1.23) based on US rates. The total-cancer SMR was somewhat higher based on New Mexico rates (SMR 1.49; 95% CI 1.30–1.68) compared with US rates (SMR 1.22; 95% CI 1.07–1.38)—mainly due to the somewhat higher lung cancer SMR based on New Mexico rates (SMR 2.56; 95% CI 2.12–3.07) compared with US rates (SMR 1.65; 95% CI 1.36–1.97). Non-malignant respiratory disease mortality was nearly identical based on New Mexico rates (SMR 1.38) compared with US rates (SMR 1.42). Deaths due to external causes were lower based on New Mexico rates (SMR 0.87; 95% CI 0.69–1.08) compared with US rates (SMR 1.45; 95% CI 1.14–1.92). Other than for external causes of death, there were no appreciable differences in the SMRs.

Table 3. Observed and expected numbers of deaths and standardised mortality ratios (SMRs) among employees at uranium mills or mines near Grants, New Mexico, followed 1979–2005, by mining experience.

Mining experience	Yes				No			
No. of persons	1735				904			
Person-years of observation	40027				20937			
Cause of death (ICD9)	Obs	Exp	SMR	95% CI	Obs	Exp	SMR	95% CI
All causes of death (001–999)	541	426.4	1.27[b]	1.16–1.38	253	262.1	0.97	0.85–1.09
All malignant neoplasms (140–208)	177	121.6	1.46[b]	1.25–1.69	65	73.0	0.89	0.69–1.14
Buccal cavity and pharynx (140–149)	1	2.6	0.38	0.01–2.13	1	1.4	0.71	0.02–3.98
Oesophagus (150)	2	3.8	0.52	0.06–1.89	2	2.0	0.99	0.12–3.57
Stomach (151)	5	3.2	1.58	0.51–3.68	0	1.9	0.00	0.00–1.99
Colon (153)	9	9.9	0.91	0.42–1.73	2	6.1	0.33	0.04–1.19
Rectum (154)	1	1.9	0.52	0.01–2.90	0	1.1	0.00	0.00–3.26
Biliary passages and liver (155, 156)	6	3.2	1.85	0.68–4.02	3	1.9	1.62	0.33–4.72
Pancreas (157)	4	6.1	0.66	0.18–1.68	4	3.6	1.12	0.31–2.87
Bronchus, trachea, and lung (162)	95	43.8	2.17[b]	1.75–2.65	21	24.9	0.85	0.52–1.29
Breast (174, 175)	0	0.5	0.00	0.00–7.59	2	1.7	1.20	0.15–4.32
All uterine (179–182)	0	0.1	0.00	—	0	0.3	0.00	0.00–10.6
Other female genital organs (183–184)	0	0.1	0.00	—	2	0.5	3.94	0.48–14.2
Prostate (185)	9	8.3	1.08	0.49–2.05	4	5.8	0.69	0.19–1.76
Kidney (189.0–189.2)	3	3.4	0.89	0.18–2.61	3	1.9	1.61	0.33–4.71
Bladder and other urinary (188, 189.3–189.9)	0	2.9	0.00	0.00–1.26	4	1.9	2.15	0.59–5.50
Melanoma of skin (172)	6	2.4	2.49	0.91–5.41	0	1.3	0.00	0.00–2.87
Brain and CNS (191–192)	2	3.6	0.56	0.07–2.03	3	1.9	1.57	0.32–4.59
Thyroid and other endocrine glands (193–194)	1	0.4	2.80	0.07–15.6	0	0.2	0.00	0.00–17.8
Bone (170)	0	0.2	0.00	0.00–15.9	0	0.1	0.00	0.00–28.8
All lymphatic, haematopoietic tissue (200–208)	18	11.9	1.51	0.90–2.39	4	7.0	0.57	0.16–1.47
Non-Hodgkin lymphoma (200, 202)	4	4.9	0.82	0.22–2.11	1	2.8	0.36	0.01–1.98
Hodgkins lymphoma (201)	1	0.4	2.28	0.06–12.7	0	0.2	0.00	0.00–16.3
Leukaemia and aleukaemia (204–208)	9	4.5	2.01	0.92–3.82	3	2.7	1.12	0.23–3.28
Chronic lymphocytic leukaemia (204.1)	2	0.9	2.23	0.27–8.05	2	0.6	3.58	0.43–12.9
Leukaemia other than CLL	7	3.6	1.96	0.79–4.04	1	2.1	0.47	0.01–2.64
Multiple myeloma (203)	4	2.0	1.97	0.54–5.05	0	1.2	0.00	0.00–3.02
Pleura and peritoneum (158.8,158.9,163) and mesothelioma (ICD10 C45)[a]	1	0.5	2.14	0.05–11.9	1	0.3	3.85	0.10–21.5
AIDS (042-044, 795.8)	0	5.0	0.00[b]	0.00–0.74	0	2.0	0.00	0.00–1.86
Diabetes (250)	11	10.0	1.10	0.55–1.97	9	6.1	1.48	0.68–2.81
Mental and behavioural disorders (290–319)	8	4.9	1.65	0.71–3.25	1	3.1	0.33	0.01–1.81
Diseases of the nervous system (320–389)	14	8.3	1.69	0.92–2.83	9	5.6	1.60	0.73–3.03
Cerebrovascular disease (430–438)	16	18.3	0.88	0.50–1.42	14	13.3	1.06	0.58–1.77
All heart disease (390–398, 404, 410–429)	133	138.6	0.96	0.80–1.14	73	87.1	0.84	0.66–1.05
Non-malignant respiratory disease (460–519)	55	33.6	1.64[b]	1.23–2.13	25	23.4	1.07	0.69–1.58
Bronchitis, emphysema, asthma (490–493)	25	11.6	2.16[b]	1.40–3.19	8	7.4	1.08	0.47–2.12
Cirrhosis of liver (571)	18	10.1	1.79[b]	1.06–2.83	3	5.0	0.60	0.12–1.75
Nephritis and nephrosis (580–589)	3	4.0	0.76	0.16–2.21	3	2.8	1.08	0.22–3.17
All external causes of death (800–999)	58	35.1	1.65[b]	1.26–2.14	20	16.8	1.19	0.73–1.84
Accidents (850–949)	31	20.6	1.50[b]	1.02–2.13	15	10.1	1.48	0.83–2.45
Suicides (950–959)	21	10.2	2.06[b]	1.28–3.15	4	4.8	0.84	0.23–2.15
Unknown causes of death	12				7			

[a] There were 106 workers with 2431 person-years of follow-up whose mining experience was unknown. Their overall SMR was 0.95 (95% CI 0.61–1.42; $n = 24$) and their total-cancer SMR was 0.58 (95% CI 0.16–1.47; $n = 4$).

[b] $p < 0.05$.

Table 4. Observed and expected numbers of deaths and standardised mortality rates (SMRs) for employees at the uranium mill near Grants, New Mexico, who never worked at an underground mine and followed from 1979–2005, by whether they worked with ore or processed uranium.

Worked with ore or uranium processing activities	Likely[a]				Unlikely[b]			
No. of persons	718				186			
Person-years of observation	16 333				4604			
Cause of death (ICD9)	Obs	Exp	SMR	95% CI	Obs	Exp	SMR	95% CI
All causes of death (001–999)	220	220.1	1.00	0.87–1.14	33	42.0	0.79	0.54–1.10
All malignant neoplasms (140–208)	56	59.6	0.94	0.71–1.22	9	13.5	0.67	0.31–1.27
Buccal cavity and pharynx (140–149)	1	1.2	0.84	0.02–4.69	0	0.2	0.00	0.00–17.4
Oesophagus (150)	2	1.7	1.15	0.14–4.16	0	0.3	0.00	0.00–12.8
Stomach (151)	0	1.6	0.00	0.00–2.35	0	0.3	0.00	0.00–13.0
Colon (153)	2	5.0	0.40	0.05–1.44	0	1.0	0.00	0.00–3.55
Rectum (154)	0	0.9	0.00	0.00–3.90	0	0.2	0.00	0.00–19.8
Biliary passages and liver (155, 156)	3	1.5	1.94	0.40–5.67	0	0.3	0.00	0.00–11.9
Pancreas (157)	4	2.9	1.37	0.37–3.49	0	0.6	0.00	0.00–5.80
Bronchus, trachea, and lung (162)	18	20.6	0.88	0.52–1.38	3	4.3	0.70	0.14–2.04
Breast (174, 175)	0	0.5	0.00	0.00–7.13	2	1.2	1.73	0.21–6.26
All uterine (179–182)	0	0.1	0.00	0.00–36.3	0	0.2	0.00	0.00–14.9
Other female genital organs (183–184)	0	0.1	0.00	0.00–27.0	2	0.4	5.39	0.65–19.5
Prostate (185)	3	5.1	0.59	0.12–1.71	1	0.7	1.47	0.04–8.18
Kidney (189.0–189.2)	3	1.6	1.92	0.40–5.62	0	0.3	0.00	0.00–12.3
Bladder and other urinary (188, 189.3–189.9)	4	1.6	2.50	0.68–6.40	0	0.3	0.00	0.00–14.1
Melanoma of skin (172)	0	1.1	0.00	0.00–3.46	0	0.2	0.00	0.00–16.9
Brain and CNS (191–192)	3	1.6	1.93	0.40–5.63	0	0.4	0.00	0.00–10.4
Thyroid and other endocrine glands (193–194)	0	0.2	0.00	0.00–22.3	0	0.0	0.00	—
Bone (170)	0	0.1	0.00	0.00–34.7	0	0.0	0.00	—
All lymphatic, haematopoietic tissue (200–208)	4	5.8	0.69	0.19–1.77	0	1.2	0.00	0.00–3.03
Non-Hodgkin lymphoma (200, 202)	1	2.3	0.43	0.01–2.40	0	0.5	0.00	0.00–7.40
Hodgkin lymphoma (201)	0	0.2	0.00	0.00–19.7	0	0.0	0.00	—
Leukaemia and aleukaemia (204–208)	3	2.2	1.35	0.28–3.96	0	0.5	0.00	0.00–8.13
Chronic lymphocytic Leukaemia (204.1)	2	0.5	4.21	0.51–15.2	0	0.1	0.00	0.00–44.2
Leukaemia other than CLL	1	1.7	0.57	0.01–3.20	0	0.4	0.00	0.00–9.95
Multiple myeloma (203)	0	1.0	0.00	0.00–3.68	0	0.2	0.00	0.00–17.0
Pleura and peritoneum (158.8,158.9,163) and mesothelioma (ICD10 C45)	1	0.2	4.60	0.12–25.6	0	0.0	0.00	—
AIDS (042-044, 795.8)	0	1.8	0.00	0.00–2.08	0	0.2	0.00	0.00–17.9
Diabetes (250)	8	5.0	1.62	0.70–3.18	1	1.1	0.89	0.02–4.98
Mental and behavioural disorders (290–319)	1	2.6	0.38	0.01–2.12	0	0.4	0.00	0.00–8.30
Diseases of the nervous system (320–389)	8	4.6	1.73	0.75–3.40	1	1.0	1.00	0.03–5.54
Cerebrovascular disease (430–438)	12	11.2	1.07	0.55–1.87	2	2.0	0.98	0.12–3.54
All heart disease (390–398, 404, 410–429)	63	74.8	0.84	0.65–1.08	10	12.4	0.81	0.39–1.49
Non-malignant respiratory disease (460–519)	24	19.7	1.22	0.78–1.81	1	3.7	0.27	0.01–1.51
Bronchitis, emphysema, asthma (490–493)	8	6.0	1.34	0.58–2.64	0	1.5	0.00	0.00–2.53
Cirrhosis of liver (571)	3	4.2	0.72	0.15–2.09	0	0.8	0.00	0.00–4.58
Nephritis and nephrosis (580–589)	3	2.3	1.30	0.27–3.79	0	0.5	0.00	0.00–8.15
All external causes of death (800–999)	17	14.3	1.19	0.69–1.90	3	2.4	1.23	0.25–3.59
Accidents (850–949)	13	8.6	1.51	0.80–2.58	2	1.5	1.36	0.16–4.90
Suicides (950–959)	3	4.1	0.73	0.15–2.14	1	0.7	1.47	0.04–8.19
Unknown causes of death	6				1			

[a] Mill worker with potential exposure to uranium ore and/or uranium processing activities, e.g., yellowcake drying.
[b] Workers employed at mill but with unlikely or minimal exposure to uranium ore or uranium processing activities, e.g., clerk or accountant.

4. Discussion

Underground uranium miners in the vicinity of Grants, New Mexico were found to be at statistically significant increased risk of dying from lung cancer, non-malignant respiratory disease, cirrhosis of the liver and external causes of death, similar to the findings of previous occupational studies of New Mexico and Colorado plateau miners (Samet *et al* 1984a, 1991, Roscoe *et al* 1995, Roscoe 1997). The increase in lung cancer is likely attributable to the high levels of radon and radon decay products in these early mines coupled with heavy smoking habits among miners (Lundin *et al* 1971, Whittemore and McMillan 1983, Hornung and Meinhardt 1987, Samet *et al* 1991). The increase in non-malignant respiratory disease, including pneumoconiosis, may be related in part to high levels of mining dusts, such as quartz (silica) present in the mines (Samet *et al* 1984b, 1991), as well as radon decay products, diesel exhaust and excessive tobacco use (Archer *et al* 1976). Increases in deaths from cirrhosis of the liver may be related to lifestyle factors of the early mining populations such as heavy alcohol consumption. Accidental deaths while on the job were not infrequent. An association with deaths from diseases of the nervous system for all workers combined was of borderline statistical significance and may be a chance finding. Interestingly, a healthy worker effect (Howe *et al* 1988) was not apparent in this miner population as indicated by the near normal rates of heart disease, cerebrovascular disease and most other conditions.

Although there are many studies of uranium miners (Lubin *et al* 1995, NRC 1999), there are few studies of uranium millers (Pinkerton *et al* 2004, Boice *et al* 2007b). Thus it is of interest that the 718 workers with the highest potential for exposure to uranium ore and processing activities were not found to be at increased risk of any of the diseases of *a priori* interest—based on possible associations seen in other studies and on knowledge of the likely distribution of uranium within the body once inhaled or ingested. No statistically significant increases were found for kidney disease, liver disease, non-malignant respiratory disease, lung cancer, bone cancer or non-Hodgkin lymphoma.

Table 5 compares the findings of the current study of uranium mill workers with the two other studies of mill workers at the Uravan mill in Colorado (Boice *et al* 2007b) and at the seven mills included in the NIOSH study of Colorado Plateau workers (Pinkerton *et al* 2004). The latter two studies are not independent since the Uravan mill was included in the NIOSH study. The general patterns of mortality are consistent across the three studies: there is no increase in all-cause mortality or all-cancer mortality, and cancer of the lung is increased in two studies but the increases were not statistically significant. An association between exposure to uranium and lung cancer has not been established in any study of uranium millers or uranium workers (IOM 2001).

No statistically significant associations were seen for cancers of the kidney, liver, bone or lymphoma (table 5). The risk of bladder cancer was increased in our study but was decreased in the other two series. Heart disease was below expectation in all three studies and the decreased risk was statistically significant in two of them. Non-malignant renal disease was not increased in any study at the level of statistical significance. The only statistically significant elevation was for non-malignant respiratory disease observed in the large NIOSH study (SMR 1.43; $n = 100$) but not in the Uravan study (SMR 0.99; $n = 24$) or in the current study (SMR 1.22; $n = 24$). Most (54%) of the uranium mill workers in the NIOSH study had begun work prior to 1955 when the potential for exposure to silica, uranium ore, vanadium and other mill contaminants was assumed higher than in later years. The Grants uranium mill began in 1955 but the Uravan mill began operations in 1936 and 42% were hired prior to 1955. The NIOSH investigators, however, were cautious in concluding that non-malignant respiratory disease was due to milling activities because of the inverse association seen with duration of

Table 5. Observed and expected numbers of deaths and standardised mortality ratios (SMRs) among mill workers near Grants, New Mexico (current study), Colorado (Boice *et al* 2007b), and the Colorado Plateau (Pinkerton *et al* 2004).

Worked with ore or uranium processing	Grants New Mexico Mill[a]				Uravan Colorado Mill[a]				7 Colorado Plateau Mills[b]			
No. of persons	718				450				1484			
Person-years of observation	16 333				9294				49 925			
Calendar years of mill operation	1958–1990				1936–1984				<1940–1970+			
Calendar years of follow-up	1979–2005				1979–2004				1940–1998			
Cause of death (ICD9)	Obs	Exp	SMR	95% CI	Obs	Exp	SMR	95% CI	Obs	Exp	SMR	95% CI
All causes of death (001–999)	220	220.1	1.00	0.87–1.14	186	233.6	0.80[c]	0.69–0.92	810	877.7	0.92[c]	0.86–0.99
All malignant neoplasms (140–208)	56	59.6	0.94	0.71–1.22	48	57.6	0.83	0.62–1.11	184	204.1	0.90	0.78–1.04
Buccal cavity and pharynx (140–149)	1	1.2	0.84	0.02–4.69	1	1.0	0.96	0.02–5.37	2	5.06	0.40	9.05–1.43
Oesophagus (150)	2	1.7	1.15	0.14–4.16	0	1.5	0.00	0.00–2.51	1	5.06	0.20	0.01–1.10
Colon (153)	2	5.0	0.40	0.05–1.44	0	5.3	0.00	0.00–0.70	12	19.0	0.63	0.33–1.11
Rectum (154)	0	0.9	0.00	0.00–3.90	1	0.9	1.06	0.03–5.91	2	4.77	0.42	0.05–1.51
Biliary passages and liver (155,156)	3	1.5	1.94	0.40–5.67	1	1.4	0.71	0.02–3.94	4	5.04	0.79	0.22–2.03
Pancreas (157)	4	2.9	1.37	0.37–3.49	3	2.7	1.10	0.23–3.20	6	10.3	0.58	0.21–1.27
Bronchus, trachea, and lung (162)	18	20.6	0.88	0.52–1.38	24	19.1	1.26	0.81–1.87	78	68.9	1.13	0.89–1.41
Prostate (185)	3	5.1	0.59	0.12–1.71	7	6.9	1.01	0.41–2.08	15[c]	19.7	0.76	0.43–1.26
Kidney (189.0–189.2)	3	1.6	1.92	0.40–5.62	1	1.4	0.74	0.02–4.10	4	4.96	0.81	0.22–2.06
Bladder and other urinary (188, 189.3–189.9)	4	1.6	2.50	0.68–6.40	1	1.9	0.54	0.01–2.99	5[d]	11.0	0.45	0.15–1.06
Bone (170)	0	0.1	0.00	0.00–34.7	0	0.1	0.00	0.00–39.3	Not given			
All lymphatic, haematopoietic tissue (200–208)	4	5.8	0.69	0.19–1.77	3	5.5	0.55	0.11–1.60	21	18.7	1.12	0.69–1.71
Non-Hodgkin lymphoma (200, 202)	1	2.3	0.43	0.01–2.40	1	2.1	0.47	0.01–2.63	4	2.29	1.74	0.48–4.46
Hodgkin lymphoma (201)	0	0.2	0.00	0.00–19.7	1	0.1	6.94	0.17–38.7	4	1.21	3.30	0.90–8.43
Leukaemia and aleukaemia (204–208)	3	2.2	1.35	0.28–3.96	1	2.2	0.46	0.01–2.54	5	7.62	0.66	0.21–1.53
Diabetes (250)	8	5.0	1.62	0.70–3.18	4	4.7	0.86	0.23–2.19	10	14.6	0.68	0.33–1.26

Table 5. (Continued.)

Worked with ore or uranium processing	Grants New Mexico Mill[a]				Uravan Colorado Mill[a]				7 Colorado Plateau Mills[b]			
No. of persons	718				450				1484			
Person-years of observation	16 333				9294				49 925			
Calendar years of mill operation	1958–1990				1936–1984				<1940–1970+			
Calendar years of follow-up	1979–2005				1979–2004				1940–1998			
Cause of death (ICD9)	Obs	Exp	SMR	95% CI	Obs	Exp	SMR	95% CI	Obs	Exp	SMR	95% CI
All heart disease (390–398, 404, 410–429)	63	74.8	0.84	0.65–1.08	65	85.9	0.76[e]	0.58–0.97	293	349.0	0.84[e]	0.75–0.94
Non-malignant respiratory disease (460–519)	24	19.7	1.22	0.78–1.81	24	24.4	0.99	0.63–1.47	100	70.2	1.43[e]	0.65–1.05
Cirrhosis of liver (571)	3	4.2	0.72	0.15–2.09	0	2.9	0.00	0.00–1.27	Not given			
Nephritis and nephrosis (580–589)	3	2.3	1.30	0.27–3.79	3	2.7	1.09	0.23–3.19	9	7.07	1.28	0.59–2.44
All external causes of death (800–999)	17	14.3	1.19	0.69–1.90	7	10.1	0.69	0.28–1.43	47	37.2	1.26	0.93–1.68
Unknown causes of death	6				1				16			

[a] Mill workers with potential exposure to uranium ore and/or uranium processing activities based on job titles, e.g., yellowcake drying. Uravan mill values from table 6 of Boice *et al* (2007b).

[b] Cause of death categories are presented that are as similar as possible to those in the other two mill worker studies. Values from table 2 of Pinkerton *et al* (2004). The Uravan mill was included in the NIOSH study so the results are not independent. The Grants, New Mexico mill was not included in the NIOSH study.

[c] Male genital (ICD9 185–187).

[d] All urinary (ICD9 188–189).

[e] $p < 0.05$.

employment. Similar to lung cancer, non-malignant respiratory disease has not been established as a consequence of uranium exposure in any study (IOM 2001).

Ours is one of the few studies of uranium workers that include both underground miners exposed to radon, and uranium millers exposed to ore and milling products. These two types of uranium exposure showed very different risk patterns. Underground mining, with increased exposure to radon gas and its decay products, was clearly associated with increased risk of lung cancer, but no other cancer, consistent with previous studies of miners (Darby *et al* 1996, NRC 1999). In contrast, uranium milling and exposure to uranium ore was not associated with any cancer or non-malignant condition, also consistent with previous studies (Waxweiler *et al* 1983, Pinkerton *et al* 2004, Boice *et al* 2007b). Uranium is not considered carcinogenic in humans (IARC 2001, ATSDR 1999), in large part because it is not very radioactive given its long half-life of billions of years. The hazard associated with uranium exposure is due primarily to its chemical properties as a heavy metal, and kidney disease is the outcome of most concern following excessive exposure (Leggett 1989, ATSDR 1999). Apparently, such exposure was not sufficient to result in a detectable increase of renal disease among mill workers in our study or the two previous studies, consistent with practically all other studies that find no association between exposure to uranium and clinically important renal dysfunction (IOM 2001). Our findings of excess lung cancer among miners but not among millers are also consistent with a recent study of uranium millers and miners in Colorado (Boice *et al* 2007b).

4.1. Studies of environmental exposure to uranium

Although uranium can enter the body by ingestion of food and water or by inhalation of uranium-containing dust, environmental exposures have not been associated with detrimental health effects (Taylor and Taylor 1997). Epidemiologic studies of the ingestion of high levels of uranium, radium, radon and other radionuclides in drinking water in Finland have provided no evidence for increased rates of cancers of the bladder, kidney or stomach, or of leukaemia (Auvinen *et al* 2002, 2005, Kurttio *et al* 2006b). High intakes of natural uranium in drinking water have been linked to subtle effects on bone formation but only in males and not females and there was no evidence of overt bone disease (Kurttio *et al* 2005). Uranium millers and miners in the current study also were not found to be at increased risk for cancers of the bone, bladder, kidney and stomach or leukaemia.

Several descriptive correlation studies of populations living near uranium milling and mining facilities have been conducted in Texas (Boice *et al* 2003a) and in Colorado (Mason *et al* 1972, Boice *et al* 2007a). No association with any cancer was observed except for lung cancer in the Colorado study which was attributed, and then confirmed, to be most likely due to an occupational exposure to radon among underground miners residing in the area (Boice *et al* 2007b). The extensive uranium milling and mining activities in Texas were not associated with increased lung cancer mortality in all likelihood because only surface and *in situ* mining, and not underground mining, were performed and high exposures to radon were not possible (Boice *et al* 2003a). Similar studies of cancer incidence and mortality in populations residing within about one mile of nuclear fuel processing and uranium fabrication facilities in Pennsylvania have also failed to reveal increased cancer rates (Boice *et al* 2003b, 2003c).

4.2. Kidney disease

The possible chemical toxicity of uranium, a heavy metal, is considered more important for human health than the risk of cancer from its radioactive properties (Taylor and Taylor 1997, Leggett 1989). No statistically significant increase in renal disease, however, was found in

the current study (3 observed versus 2.3 expected) nor in the NIOSH study of uranium millers of the Colorado plateau (9 observed versus 7.07 expected). The NIOSH study also reported that the risk of end-stage renal disease was not increased (Pinkerton *et al* 2004). Consistent with these results, renal disease was not increased among 450 millers in Uravan, Colorado (3 observed versus 2.7 expected) although many of these workers may have been included in the larger NIOSH investigation (Boice *et al* 2007b). Other studies of workers exposed to uranium have not found increases in kidney disease (Roscoe 1997, Russell *et al* 1996). One study of 39 uranium mill workers, however, reported changes in kidney function that suggested mild renal damage and, conversely, other changes that suggested improved glomerular function, but no apparent kidney disease (Thun *et al* 1985). Similarly, high levels of uranium in drinking water in Finland have produced subtle changes in some measures of kidney function but not kidney disease (Kurttio *et al* 2002, 2003, Kurttio *et al* 2006a). Studies of Gulf War veterans exposed to depleted uranium and of workers exposed to enriched uranium also find no evidence of clinically important renal dysfunction (IOM 2001, McDiarmid *et al* 2007). Consistent with these observations, we found no increase in mortality from non-malignant kidney disease among uranium millers and miners of Grants, New Mexico (6 observed deaths versus 7.0 expected).

4.3. Studies of New Mexico underground miners

A previous study of underground miners in New Mexico evaluated cancer and non-cancer mortality (Samet *et al* 1991). The only statistically significant excess was of lung cancer mortality (SMR 4.00; 95% CI 3.1–5.1; $n = 68$) attributed to the high concentrations of radon gas and radon decay products in unventilated underground mines and excessive tobacco use. Lung cancer increases were also seen among Navajo miners (Samet *et al* 1984a, Roscoe *et al* 1995). Increases in non-malignant respiratory diseases may have been partially due to high levels of silica dust causing pneumoconiosis and associated lung conditions (Samet *et al* 1984b). Our study of 1735 uranium miners revealed a statistically significant excess of lung cancer (SMR 2.17; $n = 95$) that was consistent with these previous investigations, as was the statistically significant increase in non-malignant respiratory disease (SMR 1.64; $n = 55$), attributable, perhaps, to silica, radon and other mine exposures and excessive tobacco use (IOM 2001). Statistically significant increases in external causes of death from accidents and suicides were seen in our study (SMR 1.65) and the previous study (SMR 1.5) of miners from New Mexico (Samet *et al* 1991) indicating the hazardous nature of underground mining and, perhaps, the characteristics of persons who choose mining as a profession.

4.4. Studies of cohorts exposed to uranium

During the early years of uranium processing, enrichment, manufacturing and milling, aboveground workers had the potential to inhale or ingest uranium dust with minimal exposure to radon gas (UNSCEAR 2008). Well over 120 000 of these workers have been studied and, overall, no consistent elevations in cancer risk were observed (Harley *et al* 1999, Royal Society 2001, IOM 2001, McGeoghegan and Binks 2000a, 2000b, 2006). Studies of workers with estimates of organ doses from uranium intakes also failed to find clear evidence of dose-response relationships (Dupree *et al* 1995, Boice *et al* 2006a, 2006b). In contrast to these negative studies of cancer risk among workers exposed to uranium dust and compounds, studies of underground uranium miners have revealed consistent and substantial increases in lung cancer attributed to radon gas and its decay products (NRC 1999).

4.5. Strengths and limitations

Strengths of our occupational study include the cohort design, the complete roster of all workers employed by a large uranium milling and mining company, and the long follow-up of the workers of up to 50 yrs. We also were able to distinguish between workers employed as underground miners, uranium millers or in both occupations. Limitations of the study include the relatively small number of workers within specific exposure categories and the lack of measurements of actual radiation exposure. Smoking histories also were not known.

Although the number of workers was relatively small (2930 overall and 2745 alive in 1979), the follow-up was long with 65% followed for more than 30 yrs after date of first employment and 38% followed for more than 40 yrs. Further, the number of deaths was sufficient to reveal increases for several causes of death; for example, among uranium miners we found statistically significant elevations of two-fold or less for lung cancer, non-malignant respiratory disease and cirrhosis of the liver.

For non-miners, the sample size was also sufficient to rule out relatively small increases in risk. For example, the SMR for total cancer, based on 56 deaths, was 0.94 (95% CI 0.71–1.22), indicating that with 95% confidence mortality elevations greater than 1.22 can be excluded. Relatively low SMRs for most diseases of *a priori* interest could be excluded, i.e., the upper 95% confidence limit was 1.38 for lung cancer, 1.81 for non-malignant respiratory disease and 2.09 for liver cirrhosis.

Although there were no measurements of individual exposures to uranium, silica, vanadium, radon, radium or other radionuclides, we could classify workers with regard to type of employment (underground mine and/or uranium mill), length of employment and, based on job title, likely exposure to ore or uranium processing activities. These occupational classifications allowed us to infer risks associated with specific types of exposures. For example, the statistically significant increase in lung cancer was restricted to workers employed as underground miners exposed to radon and radon decay products, whereas the non-mining population was not at statistically significant increased risk of dying from any cause. Thus, our study provides little support for the hypothesis that non-mining jobs may increase cancer risk. Furthermore, there was no evidence that those employed in non-mining jobs for greater than 5 yrs (i.e., for those who might have received the greatest exposure to uranium ore and mill effluents) experienced greater risks than those potentially exposed for shorter times.

Exposure misclassification is possible because employment in other regions of the country was not generally known. Prior work for other companies was not always recorded, and work histories after leaving the Grants, New Mexico area were in large part not available. The sample of worker records sent to NIOSH, for example, indicated that up to 17% of the millers might have had unrecognised employment underground as uranium miners. Such unrecognised underground exposures to radon and radon progeny could be substantial with cumulative concentrations over 100 WLM (Boice *et al* 2007b), compared with the yearly non-occupational exposure to radon of about 0.2 WLM. In addition to work as underground miners, some millers were also found to have worked at other uranium mills in Arizona, Colorado and other states.

Low risks for heart disease and cerebrovascular disease are often reported in occupational studies and ascribed to the 'healthy worker effect' associated with selection for employment and for continued employment (Monson 1986, Howe *et al* 1988). The healthy worker effect often diminishes with time, especially for cancer deaths. While a healthy worker effect was suggested among millers who had a lower risk of death from heart disease compared with the general population, no similar effect was seen among miners.

The study is of mortality and not incidence of disease for which the number of events and quality of diagnoses would be expected to be higher. Most of the diseases of interest, e.g., lung cancer and bone cancer, however, have a high fatality rate so that mortality would reflect incidence fairly closely. Diseases that have a low fatality rate can be evaluated in mortality studies, although the statistical power to identify a significant increase in risk might be lower than for an incidence survey because of the smaller number of events.

Because of the mobility of the workforce, mortality rates for the entire United States were used to compute expected numbers of deaths since use of New Mexico rates likely would have overestimated the SMRs. Many workers after terminating employment left New Mexico and spent substantial portions of their lives living in other states. Just over 55% of the 818 deaths occurring after 1978 happened outside the state of New Mexico. Because New Mexico rates of mortality are generally lower than for the United States as a whole, the computed expected numbers accordingly would be lower and the SMRs higher than if based on comparisons with the United States. The all-cause SMR among all workers based on New Mexico rates was 1.19 compared with the SMR of 1.15 based on United States rates, although there were wider differences for specific cancer sites such as of the lung. A 'true' SMR is likely somewhere between that computed using New Mexico rates and that computed using United States rates. Fortunately, comparisons did not differ greatly and no changes in study conclusions would have resulted had New Mexico mortality rates been used.

Tobacco use was not known for individual workers. This important carcinogenic exposure causes nearly 90% of all lung cancers, and significant percentages of cancers of the kidney, oral cavity and pharynx and non-malignant respiratory disease (Surgeon General 2004, ACS 2008). Previous studies of workers occupationally exposed to uranium in New Mexico indicate that they tend to be heavy smokers (Samet *et al* 1991), although not the Navajo miners (Samet *et al* 1984a, Roscoe *et al* 1995).

The mortality before 1979 from all causes (SMR 1.24 based on US rates and 1.09 based on NM rates, $n = 185$) was similar to that after 1978 (SMR 1.15). However, SMRs for specific causes of death could not be determined because of the incomplete collection of death certificates in the early years before the National Death Index began. Although death certificates were sought for all 185 deaths occurring before 1979, information on state of death was so incomplete that only 105 (or 56.8%) certificates were obtained. Most of the acquired death certificates were from the state of New Mexico (75 or 71.4%); the other certificates resulted from requests made to 26 other states. Most of these early deaths with known causes were due to car and mine accidents, gun shot wounds and homicides ($n = 40$ or 21.6%). Lung cancer deaths were elevated, i.e., 14 lung cancer deaths occurred in contrast to 9.8 expected computed based on the person-years of observation between date of first employment to January 1, 1979. There was only one death each attributed to kidney cancer and leukaemia and there was no deaths from lymphoma. The consistency of the pre-1979 findings with those for deaths after 1978, i.e., no apparent increase overall and only lung cancer being significantly elevated, indicates that the incomplete cause of death information for these early deaths and their exclusion from study is unlikely to have biased study conclusions with regard to late effects from mining or milling exposures.

4.6. Conclusions

Consistent with prior studies of underground miners in New Mexico, the lung cancer excess among miners in our study is likely due to radon and radon decay products. In contrast, exposure to uranium dust and other mill products had little or no effect upon disease rates, consistent with current understanding (ATSDR 1999, IOM 2001, IARC 2001). The absence

of statistically significant excesses of leukaemia is as expected since uranium ore and mill products are not very radioactive and the emission of penetrating gamma radiation is low. This is one of the few studies of both uranium miners and uranium millers within the same workforce and the patterns of cancer clearly differ. Underground uranium miners were exposed to high levels of radon decay products and lung cancer resulted, but no other malignancy. Uranium millers were exposed to uranium dust, ore and mill effluents, but exposure to this heavy metal and mill processes did not increase the number of lung cancers or non-malignant diseases of the respiratory system and urinary tract. Our study adds to the growing body of evidence that uranium ore and uranium compounds are not human carcinogens, and that, in comparison to radon, uranium dust is not a major health hazard.

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Appendix 8

UMETCO Minerals Corporation
Soil Radiometric Data
UMETCO Gas Hills Site

Non-Random Background Soil Radiometric Data

SAMPLE I.D.#	U-Nat (pCi/g)	Ra226 pCi/g	Ra226 Prec. +/-	Th230 pCi/g	Th230 Pec. +/-	Pb210 pCi/g	Pb210 Prec. +/-
SS # 1; 0-6"	0.9	1.6	0.5	< 0.02		0.2	0.2
SS # 1; 6-12"	0.8	1.1	0.3	< 0.02		< 0.10	
SS # 2; 0-6"	0.07	1.3	0.2	2.3	0.7	0.3	0.3
SS # 2; 6-12"	0.06	1.3	0.2	< 0.02		0.5	0.4
SS # 3; Road Bed	37.4	119	0.2	177	5.8	89.3	3.2
SS # 4; 0-6"	0.05	1	1	< 0.02		0.3	0.3
SS # 4; 6-12"	0.6	1.1	0.3	< 0.02		0.3	0.3
SS # 5; 0-6"	1.1	1.4	0.3	< 0.02		< 0.10	
SS # 5; 6-12"	1.2	1.7	0.3	< 0.02		1.1	0.8
SS # 6; 0-6"	1.1	1.6	0.3	< 0.02		< 0.10	
SS # 6; 6-12"	1.4	1.6	0.3	< 0.02		< 0.10	
SS # 7; 0-6"	2.3	1.7	0.3	< 0.02		0.8	0.8
SS # 7; 6-12"	2.9	1.9	0.3	< 0.02		0.3	0.3
SS # 8; 0-6"	1.1	1.5	0.3	< 0.02		0.4	0.4
SS # 8; 6-12"	0.9	0.8	0.1	< 0.02		0.2	0.2
SS # 9; 0-6"	1.65	15.4	1	0.5	0.1	< 0.01	
SS # 9; 6-12"	0.66	7.7	0.8	0.4	0.1	< 0.01	
SS # 10; 0-6"	3.06	38.4	1.6	1.6	0.2	0.4	0.2
SS # 10; 6-12"	2.5	41	1.6	1.9	0.2	1.3	0.2
SS # 11; 0-6"	21.5	268	2.4	50.8	2.2	153	1.1
SS # 11; 6-12"	14.5	504	3.3	58.1	2.1	272	1.2
SS # 12; 0-6"	2.19	2.9	0.3	1	0.1	1.3	0.2
SS # 12; 6-12"	0.8	1.4	0.2	0.4	0.1	10.8	0.4
SS # 13; 0-6"	0.86	1.3	0.2	0.5	0.1	1.25	0.4
SS # 13; 6-12"	0.63	0.9	0.2	0.4	0.1	0.88	0.4
SS # 14; 0-6"	0.84	1	0.2	0.5	0.1	0.86	0.4
SS # 14; 6-12"	0.59	0.9	0.2	0.4	0.1	1.08	0.4
SS # 15; 0-6"	1.88	1.4	0.2	0.6	0.1	0.75	0.4
SS # 15; 6-12"	1.19	1.4	0.2	0.9	0.2	0.42	0.3
SS # 16; 0-6"	1.66	1.1	0.2	0.8	0.2	< 0.01	
SS # 16; 6-12"	2.16	0.9	0.2	0.8	0.2	1.18	0.4
SS # 17; 0-6"	1.23	1.5	0.2	1.7	0.2	1.17	0.4
SS # 17; 6-12"	1.19	1.3	0.2	0.9	0.2	< 0.01	
SS # 18; 0-6"	0.85	0.9	0.2	0.8	0.2	1.01	0.4
SS # 18; 6-12"	0.86	1.1	0.2	0.9	0.2	0.93	0.4
SS # 19; 0-6"	19.7	68.9	1.2	18	1.3	36	0.9
SS # 19; 6-12"	23.8	35.1	0.9	6.5	0.5	21.7	0.8
SS # 20; 0-6"	24.8	7.16	0.22	3.5	0.3	2.2	0.5
SS # 20; 6-12"	8.36	11.4	0.28	6.5	0.5	4.5	0.6
	0.02	0.02		0.02		0.1	
Mean:	4.85	29.58		12.99		19.56	
Median:	1.19	1.50		0.90		1.01	
Standard Deviation:	8.67	91.12		36.52		56.40	
Maximum:	37.40	504.00		177.00		272.00	
Minimum:	0.05	0.80		0.40		0.20	

Notes:
This data was collected by UMETCO Minerals Corporation
This data was provided by John Hamrick formerly of UMETCO Minerals Corporatrion now of Cotter Corporation
This data was collected from background soil sampling locations in the Gas Hills of Wyoming.
This data was collected by UMETCO Minerals Corporation to demonstrate the variability of natural background in the Gas Hills.

Appendix 9

UNITED STATES
NUCLEAR REGULATORY COMMISSION
Office of Public Affairs
Washington, D.C. 20555

No. S-28-94
Tel. 301-415-8200

Remarks by Dr. E. Gail de Planque
Commissioner, U.S. Nuclear Regulatory Commission
before the
NRC Workshop on Site Characterization for Decommissioning
Rockville, Maryland
November 29, 1994

In Search of . . . Background

It is a pleasure to be here this morning at the NRC Workshop on Site Characterization for Decommissioning. I'm so pleased to see so many in attendance because I think that the issue of decommissioning is one of the most significant issues on the Commission's plate, one that will have long lasting and far reaching impacts.

Introduction

As you know, the NRC is undergoing a lengthy process aimed at formulating radiological criteria for the decommissioning of NRC-licensed facilities. During that process, extensive discussions have focused on four possible approaches to this task: (1) establishing an annual risk or dose limit for an individual; (2) establishing an annual risk or dose goal; (3) requiring use of the best available technology; or (4) requiring return of the site to background radioactivity. While many commenters preferred a risk-based or dose-based standard, many others favored the "return-to-background" approach.

The proposed rule attempts to accommodate both groups by establishing a dose limit for release of the site of 15 millirem per year Total Effective Dose Equivalent (TEDE) for residual radioactivity distinguishable from background with further reductions As Low As Reasonably Achievable, or ALARA.

First, an aside. To make life easier, I will usually use the quantity total effective dose equivalent expressed in units of *mrem*. But for brevity's sake, I will use the term "dose" when speaking of total effective dose equivalent.

The objective expressed in the proposed rule is to cleanup up to dose levels that are indistinguishable from background. Return to background!

Sounds good, doesn't it? On the surface, this seems like a relatively easy, common-sense approach: for example, survey a nearby spot unaffected by a nuclear facility, use that radiation level as a baseline, clean up the contaminated site to that level, and . . . voila! The site is decommissioned, the method indisputable, the job completed.

But, as we all know, the devil is in the details. And in this case, the devil could produce a series of torments for those involved in returning a site to background.

I'd like to discuss some of the details with you this morning, particularly the details that are relevant to determining what background is and how it is measured. But I'd also like to place this discussion of the details within the broader context of a regulatory decision-making process.

Risk-Based Decision-Making

The decision-making process I'm referring to is "risk-based" decision-making, a process gaining popularity both in the Clinton Administration and in Congress, and widely advocated by the most recent Supreme Court member, Justice Stephen Breyer. Let me say at the outset that as far as I know this particular mode of making decisions was not followed in any rigorous way in formulating the proposed rule. Nevertheless, for reasons which I hope will be clear later in this talk, it may offer a useful framework for working out the details of a decommissioning program.

Risk-based decision-making allows for the assumption that the resources available for limiting risks are not inexhaustible and seeks to ensure that the resources which are available to society as a whole will be put to the best overall use considering risk, cost and benefit. It can be divided into three basic components as illustrated by the following Sydney Harris cartoons: (1) risk assessment, (2) selection of an acceptable level of risk, and (3) risk management. In the context of decommissioning, risk assessment is an evaluation of the hazard associated with residual radioactivity remaining at a site released for unrestricted or restricted use. Selection of an acceptable risk level involves weighing the benefits of lowering risk to a certain level against the costs and may involve comparing the risk at issue with other similar risks confronting society. Risk management consists of a regulatory process designed to keep the risk below the level found to be acceptable.

Risk Assessment

As the NRC begins to formulate a regulatory program to manage the risk associated with sites cleaned up to levels of radiation contamination that are indistinguishable from background, it might be useful to revisit Step 1 of the risk-based decision-making process: risk assessment. Perhaps this can most easily be done by reviewing the levels of radiation to which humans are typically exposed and the health consequences of those levels.

Broadly speaking, the average American's annual radiation dose is attributable to two sources: naturally occurring radiation which, in the U.S., produces about 82% of the dose, and anthropogenic radiation which produces the remaining 18%. Humans are bathed in a sea of naturally-occurring radiation which has been present since the formation of the earth. About 56% of the average annual dose is from radon and its decay products. Another 11% is from other internal sources, mainly from inhalation and ingestion of food and water which contain naturally occurring radioactive elements. The remainder is from external sources, about 7.5% from cosmic rays and about 7.5% from terrestrial gamma ray sources such as uranium, potassium, and thorium, that are present naturally in soil and rocks.

Just to complete the picture, let's look at the anthropogenic sources. About 11% of the average annual dose comes from medical x-rays, about 4% from nuclear medicine, and about 3% from consumer products such as smoke detectors. The small remainder is from fallout from weapons testing, and occupational exposures at various nuclear facilities.

The proposed rule defines "background radiation" as:

> radiation from cosmic sources; naturally occurring radioactive material, including radon (except as a decay product of source or special nuclear material); and global fallout as it exists in the environment from the testing of nuclear explosive devices or from past nuclear accidents like Chernobyl which contribute to background radiation and are not under the control of the licensee.

Although naturally-occurring radiation and fallout from atmospheric weapons testing and the Chernobyl accident are present everywhere, each of these components of what I'll refer to as background, and the corresponding dose delivered, is by no means constant. Background levels fluctuate significantly due to various physical phenomena that differ from place to place and change with time at any given place. For example, over the long-term, cosmic radiation varies by about 10% over the 11 year solar cycle. Seasonal cycles produce changes in soil moisture, rainfall, snow cover, and evapotranspiration that cause variations in the dose from terrestrial gamma radiation, fallout and radon. Many sporadic geophysical phenomena, volcanic eruptions or earthquakes for example, can also introduce radioactivity into the environment.

Temporal variations can also occur over the short term. Rain, for example, will wash out radon and other radionuclides from the air causing an immediate rapid increase in dose that typically decreases exponentially after the rain stops. Doses from radon typically exhibit a diurnal cycle due to local climate conditions.

Radiation varies spatially. The dose from cosmic radiation is a function of both latitude and altitude. The population of the city of Denver, at an altitude of a mile receives an annual cosmic ray dose that is a factor of 2 higher than the U.S. average. Terrestrial gamma radiation, including fallout, varies from place to place because of differing amounts of uranium, potassium and thorium in the earth's surface material and can easily differ by a factor of 10 across the country. Granite, for example, contains higher than average uranium concentrations and

monazite sands can have particularly high concentrations of thorium. Furthermore, humans sometimes alter soil content with fertilizer which contains varying amounts of potassium-40. Spatial variations occur locally as well; the well-known Reading Prong in New Jersey provides an interesting regional example. The average annual dose from gamma radiation is approximately 50 mrem but if one resides closer to the rock formations along the prong, the annual dose can be much greater. About sixty miles away at the New Jersey shore, the gamma radiation dose levels fall to less than 10% of the average measured over the Prong.

Even in the immediate environment of a typical facility site (this happens to be Shoreham, Long Island), significant fluctuations occur (Figure 1). For this site with an annual average terrestrial gamma dose of about 35 mrem, when measured simultaneously, levels varied by more than 50% over a distance of only a mile within the site boundary, and the areas within a 4- or 5-mile radius of the site exhibited variations with even greater extremes.

This site in rural New Jersey, used as a background monitoring station, is only 50' by 200' (Figure 2). And even within such a small area, simultaneously measured terrestrial gamma radiation dose levels, which average about 125 mrem per year, differ by as much as 30% from spot to spot. That translates into differences of close to 40 mrem per year.

Other local variations occur due to the types of houses and buildings in which people live and work. Persons living in a wood frame house usually receive lower doses than persons living in an all brick house because, even though brick is a better shield of outdoor radiation, it has higher concentrations of naturally occurring radioactivity than wood. Persons working in granite and marble buildings may receive higher doses due to the radioactivity in the stone. Even moving from a rural to an urban setting may increase an individual's annual dose, due to the level of radioactivity present in concrete. The dose from cosmic rays can be measurably higher on the top floor of a high rise than on the ground floor. Measurements in a 12 story building in Manhattan indicated a cosmic ray dose on the ground floor one third that on the 12th floor, due principally to the shielding effect provided by many stories of concrete from the building in question as well as adjacent structures. In addition, a person's annual dose from radon can vary dramatically, by a factor of 10 or more, depending upon where they are and the adequacy of ventilation.

To further complicate matters, these temporal and spatial variations can be interdependent. For example, determining the average annual dose received from terrestrial gamma radiation cannot be done simply by measuring differences in soil concentration, since it is also affected by weather conditions. Moreover, usage must be considered and can result in what is often referred to as technologically enhanced natural background radiation. Finally, the actual dose to particular humans is heavily dependent upon the specific external and internal pathways of exposure.

Obviously then, there is no single number that represents the annual dose to U.S. citizens from background. But for perspective, it is useful to know that the average annual background dose for the U.S. population is about 300 mrem with about 200 mrem from radon, about 40

mrem from other internal sources, about 25 mrem from cosmic rays and about 25 mrem from terrestrial gamma rays. The average annual dose from fallout is less than 1 mrem.

However, because of the many factors that cause both spatial and temporal variations, the annual U.S. dose from background can easily range from 100 mrem for people who live in well-ventilated wooden houses on sandy soil at sea level to about 1000 mrem for people living in the Denver area, a factor of 10 (Figure 3). At the Shoreham site, annual doses from terrestrial gamma radiation differed with location alone by as much as 25 mrem per year. At the small New Jersey site, the equivalent spot to spot difference was as high as 40 mrem per year. It is in the context of these variations that the selection of 15 mrem over background as the acceptable annual dose for residual radiation from a decommissioned site must be viewed. For additional perspective, consider that we rarely choose our residences or domestic habits based on exposure to background radiation, yet the choice to live in a brick rather than a wood-frame house can increase one's annual dose by 45 or 50 mrem. A gas stove can deliver about 15 mrem per year to the lungs due to naturally occurring radioactive elements in the gas and a single flight across the U.S. yields about 4 mrem. A Denver resident can receive double the cosmic ray dose, triple the terrestrial dose, quadruple the radon dose, and a higher intake of radionuclides in drinking water compared to persons living in a coastal region--and if the house is not well ventilated the total dose could be still higher!

Selection of an Acceptable Level of Risk

To place the risk from exposure to background radiation in context, let's look at some general risks to the population. About 33% of the general population in the United States die of heart disease and about 23% die of cancer. Non-cancerous lung disease (7.7%), strokes (6.7%) and accidents (4.3%) also figure strongly as major causes of death (Figure 4). Comparing these causes of death, all of which carry a risk of greater than 1%, with the elective or accidental risks faced by selected groups or by the general population illustrates the complexity of adding societal choice to risk-based decision-making in terms of selection of an acceptable level of risk (Figure 5). Smoking one pack of cigarettes daily will result in death from a related cause for about 28% of smokers and a motorcyclist has about an 11% lifetime chance of dying in a motorcycle accident. By comparison, the average American's risk of dying in an air accident is several orders of magnitude lower, about 0.02%.

As I said earlier, the annual dose from natural background in the U.S. ranges from 100 to 1,000 mrem with an average of about 300 mrem. When relating these annual doses to risk, the risk assessment models developed by the International Commission of Radiological Protection (or ICRP) are usually applied. The ICRP performs risk assessments for both deterministic and stochastic effects of exposure to radiation based on research reports of radiation effects on tissues and animals, as well as on human epidemiology studies and modeling. For the purposes of radiation protection, the ICRP *assumes* a linear non-threshold dose-effect model and basically extrapolates to estimate the probability of harm resulting from low doses and dose rates where there is little, if any, human health effects data.

Using ICRP's method of risk assessment, the average annual 300 mrem dose from background produces a lifetime risk of fatal cancer of slightly less than 1 in 100, or approximately 0.82%. The corresponding lifetime fatal cancer risk for 100 and 1000 mrem are approximately 0.27% and 2.7%, respectively (Figure 6).

So how would an additional increment of 15 mrem change the public's risk from natural background? Looked at in isolation, 15 mrem per year over a 70-year lifetime would result in a risk of about 0.04% yet another decade lower on this log scale. When added to the risks associated with low, average, and high annual doses from background it is barely distinguishable (Figure 7). Indeed 15 mrem represents 5% of the average annual dose and is lost within the range of background which spans a factor of 10.

It is perhaps useful to note that for members of the public, the NCRP recommends an annual limit of 100 mrem for continuous exposure and an annual limit of 500 mrem for infrequent exposures due to all anthropogenic sources and recommends that ALARA be practiced below that. They further recommend that where there are multiple sources, no single source or set of sources under one control should result in an individual being exposed to more than 25 mrem annually.

What does one conclude from all of this? The limit of 15 mrem, including 4 mrem from drinking water which in itself is material for a lengthy lecture which I won't attempt to address here, carries a risk that is a small increment over the risk from background itself. Given that the risk is small and masked by the variation in the risk over the range of background doses, one must ask what all this should imply for the third or final component of risk-based decision-making, risk management.

Risk Management

The major questions for risk management are: (1) What is it that will be measured or used to represent "background" at a particular decommissioning site? (2) What will be measured to determine compliance with the 15 mrem limit? and (3) What margins of error or what uncertainties will be considered acceptable in determining compliance?

The difficulties involved in answering these questions become apparent when a site's decommissioning efforts are broken down into a series of steps and the complications that can exist with each step are examined. The overall process consists of, first, an analysis of the activities that have been performed at the site to be decommissioned; second, an assessment or survey to establish what represents background and a survey of the site to determine the degree of cleanup required; third, cleanup; fourth, a resurvey of the site; and, finally, release of the decontaminated site.

Each of these activities can be further broken down into sub-steps. For example, the person performing an analysis of the activity at the site must ask a series of questions: (1) Did the licensed activities involve single or multiple radionuclides? (2) With respect to each

radionuclide, does it also exist in background or is it only produced as a result of licensed activities at the site? (3) For each radionuclide, are there single or multiple pathways that may result in exposure to humans?

Surveying also has multiple sub-steps. Survey methods and the required number of surveys of each type must be determined to establish the background level or levels. The corresponding number of site surveys that will be necessary to establish the level of residual radioactivity on site with reasonable confidence must be determined and the background surveys and initial site surveys must then be performed.

The site is now ready for cleanup. Based on the analysis and survey results, the appropriate methods must be chosen and cleanup performed with periodic re-surveying to determine the level of progress until the release criteria are met and the site is ready for release.

Let's consider a few examples of how this process actually works. First, consider a simple example in which the residual radioactivity involves a single, non-naturally occurring nuclide. For simplicity's sake, postulate that the radionuclide has only one pathway of exposure. This will result in a single set of surveys, presumably a single method of decontamination, and a straightforward path toward releasing the site.

For a second example, let's consider a slightly more complicated scenario, involving multiple naturally occurring nuclides, at least one of which is known to result in human exposure via several pathways. This analysis is still relatively simple, but the surveys will be somewhat more complex. In this situation background will have to be established in a manner that accounts for variability, and that will differentiate quantitatively between background radiation and that produced by site activities. The clean-up may also be somewhat more complex due to the multiple nuclides and pathways of exposure.

The third scenario, unfortunately, may be the most realistic picture for most licensees, including reactor facilities. In this case, the analysis may involve a whole spectrum of radionuclides, some, but not all, of which occur in background. It may also involve a variety of interrelated pathways of human exposure. As a result, establishing background becomes much more complicated, even for a site with a detailed pre-operational survey. Multiple elements of spatial and temporal variation will complicate this scenario further, requiring a higher number of surveys and sometimes multiple methods to achieve the necessary degree of confidence. The decontamination of such a site, of course, will be correspondingly more difficult, involving multiple clean-up methods and, quite possibly, repeated attempts, with re-surveys performed as necessary until the criterion of 15 mrem above background has been met and the site is ready for unrestricted release.

How does this affect cost, certainly an element in risk-based decision-making? Survey costs alone, not even considering cleanup costs, will vary based on the complexity of the situation considering the number of surveys taken and the quality of those surveys in terms of the degree of confidence required, or level of uncertainty considered acceptable.

Consider the cost per sample of various radiation measurements likely to be used in any major decommissioning effort (Figure 8).[1] Assessing the potential radiation dose to humans for a multi-nuclide site could require a complete pathway analysis, including measurements of external gamma dose; air, soil and vegetation samples; and samples of surface water, drinking water, and precipitation. Obviously, to attempt to sample and measure every cubic meter of the relevant environment would be both impractical and prohibitively expensive. Instead, a sampling strategy must be developed combining radiation survey readings over large areas with selective sampling and analysis at representative locations, using the results of past measurement programs as appropriate.

Even with an efficient sampling strategy, however, the cost of performing surveys just to establish background can escalate sharply depending on the degree of uncertainty that is acceptable, which will directly influence both the survey methods employed and the number of surveys taken. In general, measuring smaller doses means increasing costs as more sophisticated techniques are employed.

Similarly the costs of site surveys and decontamination increase based on the background criteria employed and the level of sensitivity and confidence desired. For some radionuclides, the detection limits of standard laboratory instruments can be reached, causing the survey costs to rise dramatically as sophisticated research techniques become necessary. For naturally occurring radionuclides or those present in residual levels from weapons fallout, it may be virtually impossible to distinguish the contribution of site activities given the spatial and temporal variations in background discussed earlier.

Just as an example, consider the cost of measuring cesium-137 in soil (Figure 9).[2] At dose increments of about 30 mrem per year or higher, the cost is about $50 per sample. The cost roughly quadruples when trying to measure at levels of 10 mrem per year or less--based on the need for more sensitive laboratory methods--and increases dramatically again, to about $500 per sample, when measuring at a level of 0.3 mrem per year, which requires sophisticated research techniques. Because cesium-137 is present in residual radioactivity from weapons fallout, the typical levels and degree of variability make the cost of measuring this radionuclide at dose increments of 0.1 mrem per year more or less indeterminate.

What all this reveals is that every assessment of dose due to either natural or anthropogenic radiation will entail some degree of uncertainty. Whether that uncertainty stems from spatial or temporal variations, the limitations of the measurement technique, or the ability of the analyst to interpret data, it is still uncertainty, and it can never be entirely eliminated. Now let's review how the compliance process might work. First, background (χ_b) must be

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[1]NUREG-1496, Vol 2, "Generic Environmental Impact Statement in Support of Rulemaking on radiological Arteria for Decommissioning of NRC-Licensed Nuclear Facilities," Appendices, p. A-44, August, 1994.

[2]NUREG-1496, Vol 2, "Generic Environmental Impact Statement in Support of Rulemaking on radiological Arteria for Decommissioning of NRC-Licensed Nuclear Facilities," Appendices, p. A-53, August, 1994.

determined. But, unless it is zero, this is clearly not well-defined and carries an uncertainty (σ_0). To determine if cleanup is sufficient, the site must be surveyed to determine what remains (χ_1) which may or may not include natural background as discussed earlier. This, too, of course, carries an uncertainty (σ_1). Compliance requires that what remains after cleanup not contribute more than 15 mrem above background.

In addition, the proposed rule requires that further reductions be made As Low As Reasonably Achievable. Defining ALARA, in this framework, might be much more problematic than when working with higher, more readily measurable doses. Can ALARA be assigned a cost-per-dose-increment value, as is done for occupational exposures? Is it simply a matter of vague principle? And how will it take into consideration other risks, such as those associated with the decommissioning activities themselves? These are the questions of the risk management phase of risk-based decision-making.

Now let us return to the framework of risk-based decision-making which is premised on balancing risk, cost, and benefit. To implement the 15 mrem criterion, as well as ALARA, in this context, one needs to ask at least two fundamental questions:

1) How should both background and residual radioactivity be defined or measured in practical terms, and what degree of uncertainty will be considered acceptable? Recall from the examples of our earlier discussion that if one takes into account spatial or temporal variations of background, not to mention measurement uncertainties, the sigma may easily be of the same order as, or even multiples of, the 15 mrem criterion.

2) The second question follows naturally from the first: given that the risk associated with a 15 mrem residual dose adds very little to the risk of exposure to background and indeed is buried in the noise of the natural variations of that background, then how much money and effort should be spent not only to clean up to this level, but to assure compliance?

Conclusion

These are among the questions that we, as regulators, licensees, and members of the public must consider as we proceed toward final decommissioning rulemaking. And remember, I've only touched the surface. For example, we haven't even discussed the proposed 4 mrem criterion for the water pathway and the associated risk management scheme necessary to assure compliance. These are challenges of risk-based decision-making as we all go in search of background.

In this endeavor, I would urge that we be ever mindful of our goal as captured in the NRC's mission, that is, "to help assure that the use of nuclear materials is carried out in such a way that public health and safety, the common defense and security and environment are protected," and that we be mindful of the principles of good regulation, namely, independence,

openness, efficiency, clarity, and reliability. This is our challenge as we strive to protect the citizens of our nation and fulfill our responsibilities as stewards of our planet. I, for one, welcome the challenge, daunting as it may seem, and I look forward to the contributions and participation of all parties as we proceed toward what I hope will be rational and responsible final rulemaking.

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RELATIVE TERRESTRIAL GAMMA RADIATION LEVELS (MAY 1974)

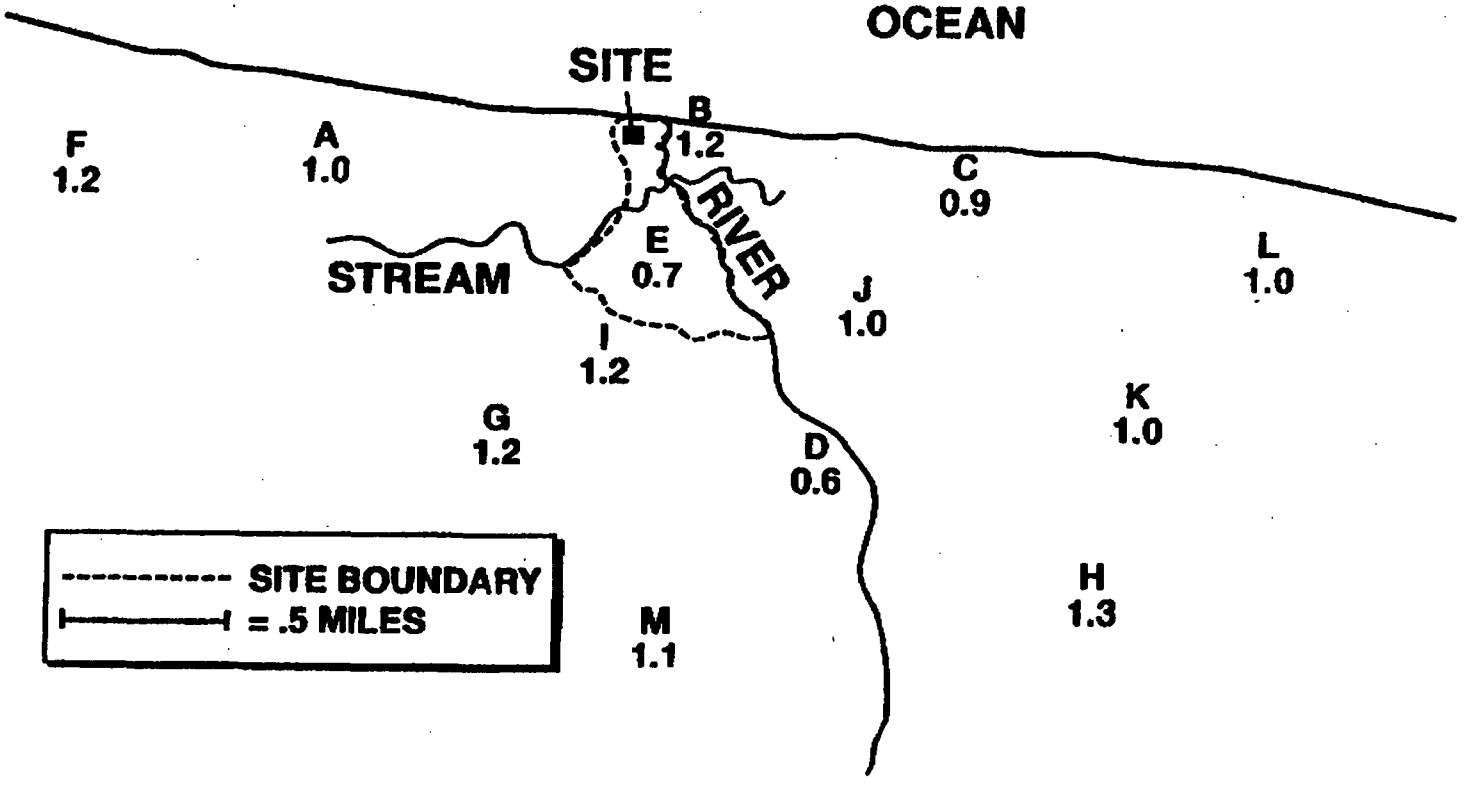


FIGURE 1

RELATIVE TERRESTRIAL GAMMA RADIATION LEVELS (SEPTEMBER 1974)

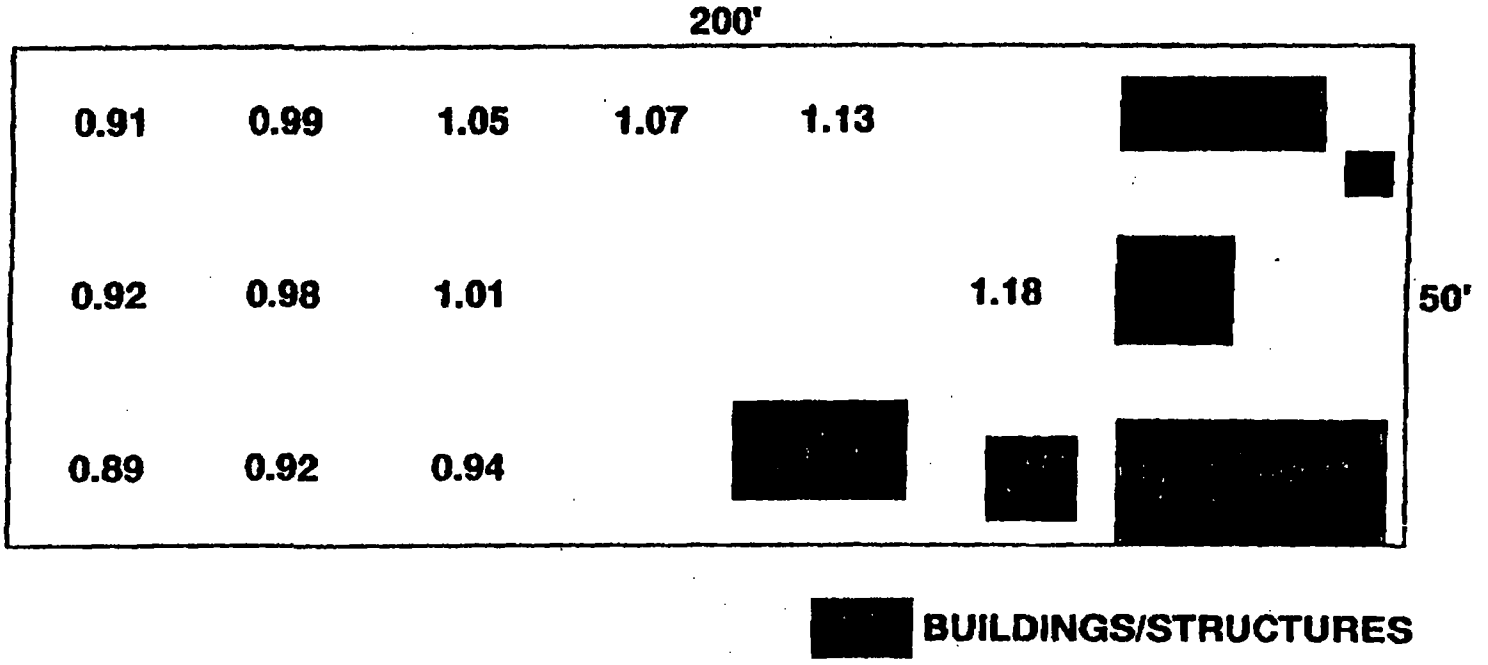
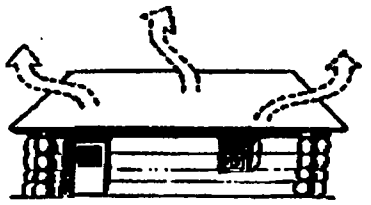


FIGURE 2

RANGE OF ANNUAL RADIATION DOSE: NATURAL SOURCES (MREM)



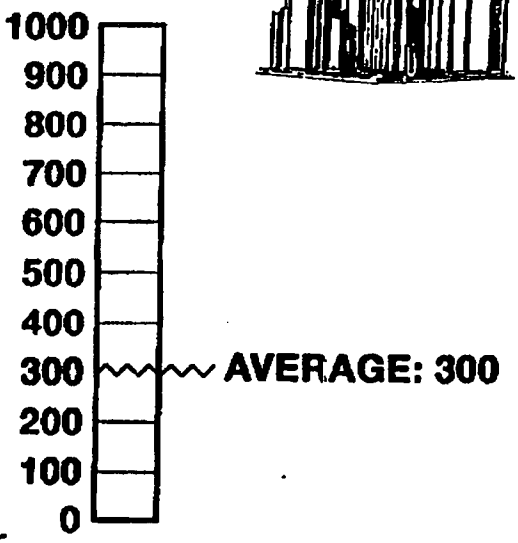


FIGURE 3

LIFETIME MORTALITY RISKS
(PERCENT OF GENERAL POPULATION)

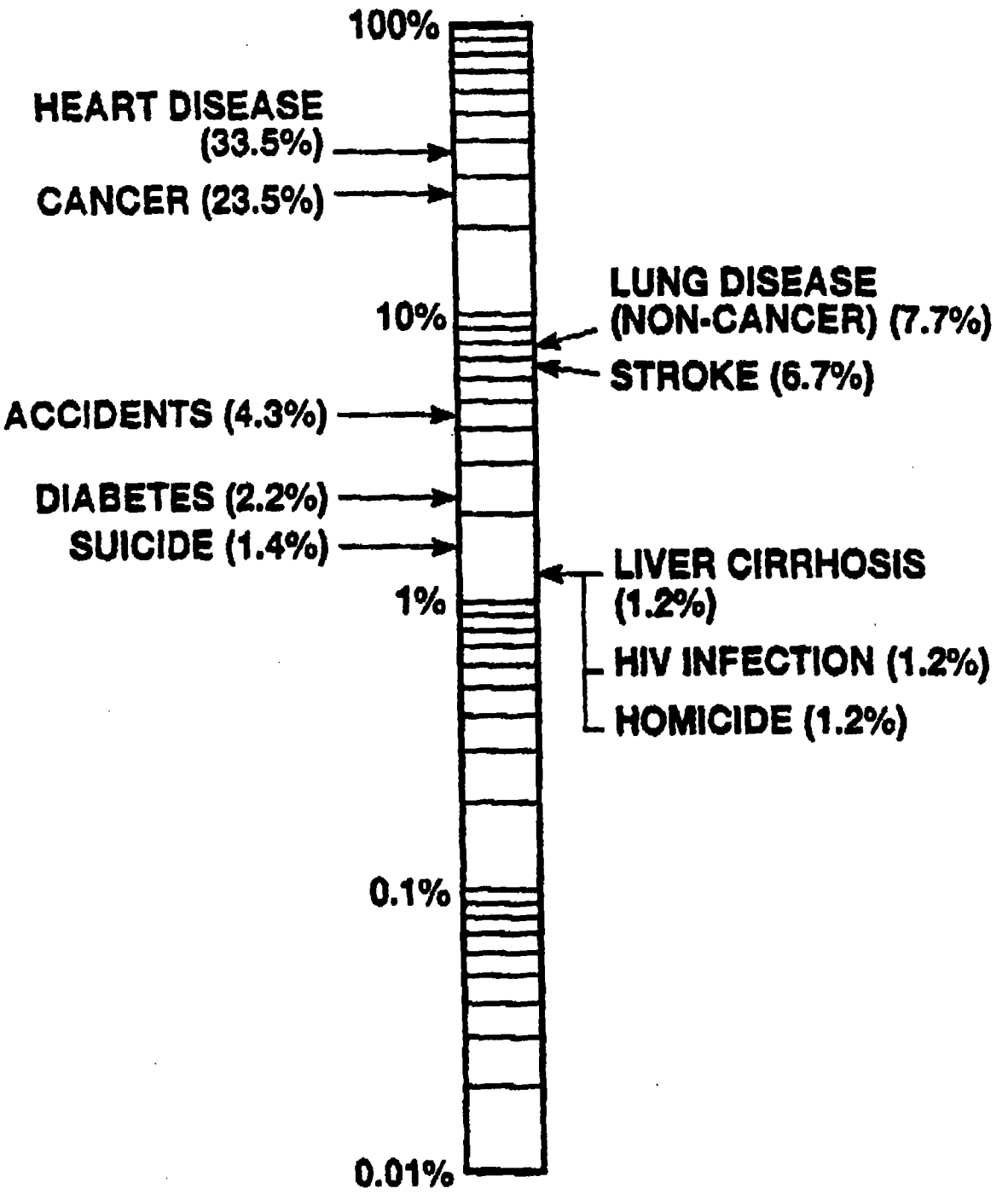
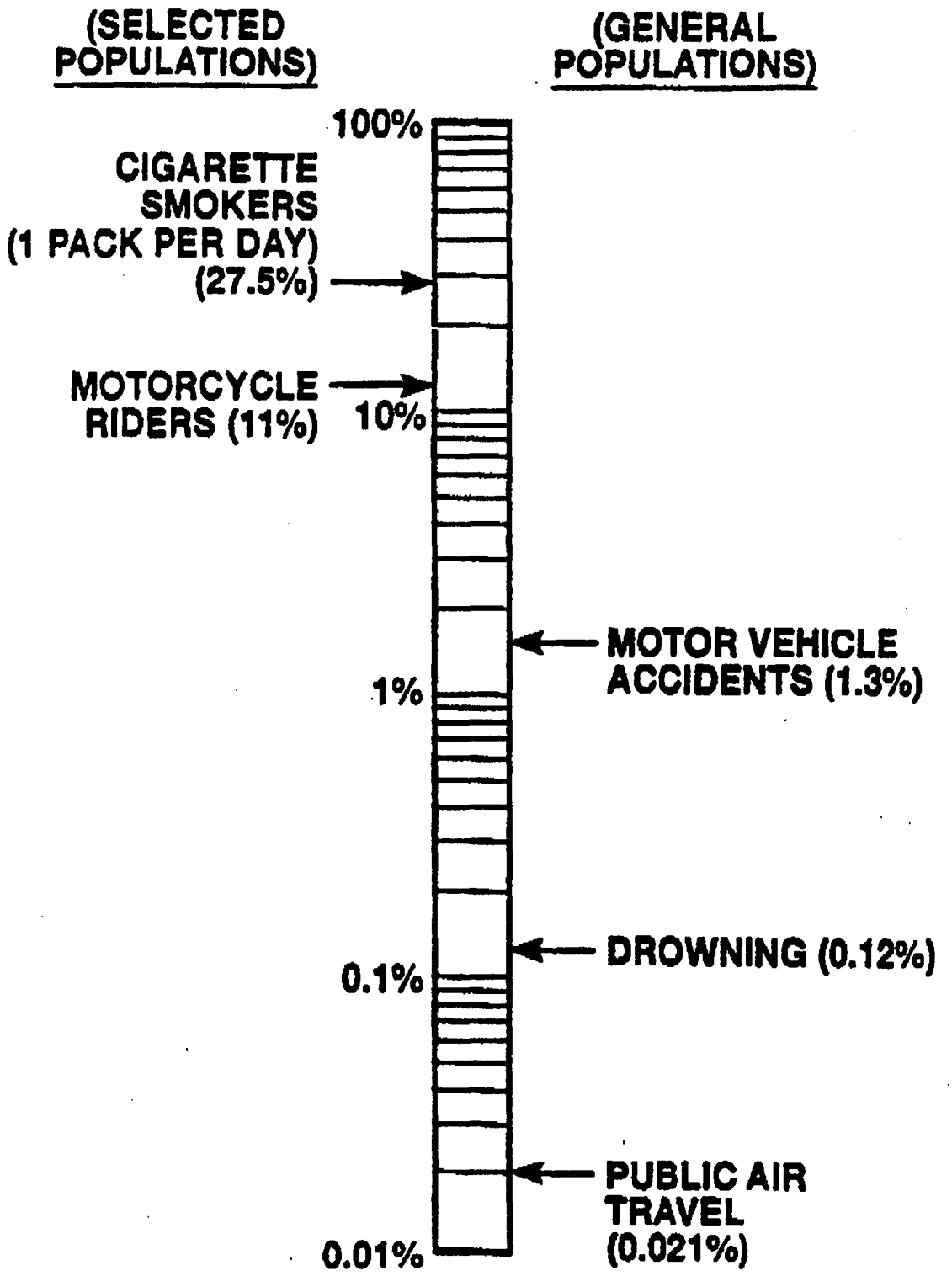
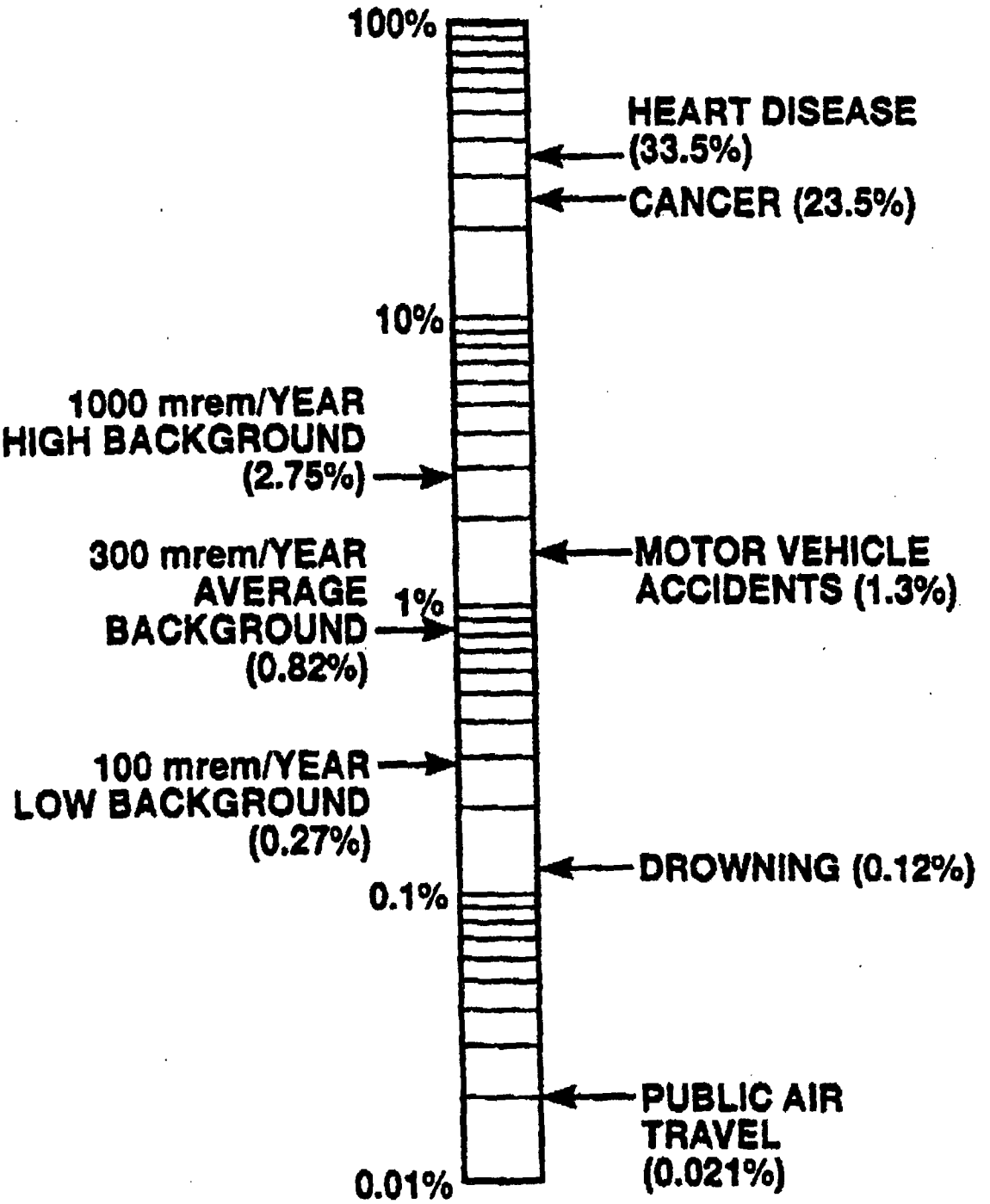


FIGURE 4

LIFETIME MORTALITY RISKS
(PERCENT)



LIFETIME MORTALITY RISKS
(PERCENT)



LIFETIME MORTALITY RISKS
(PERCENT)

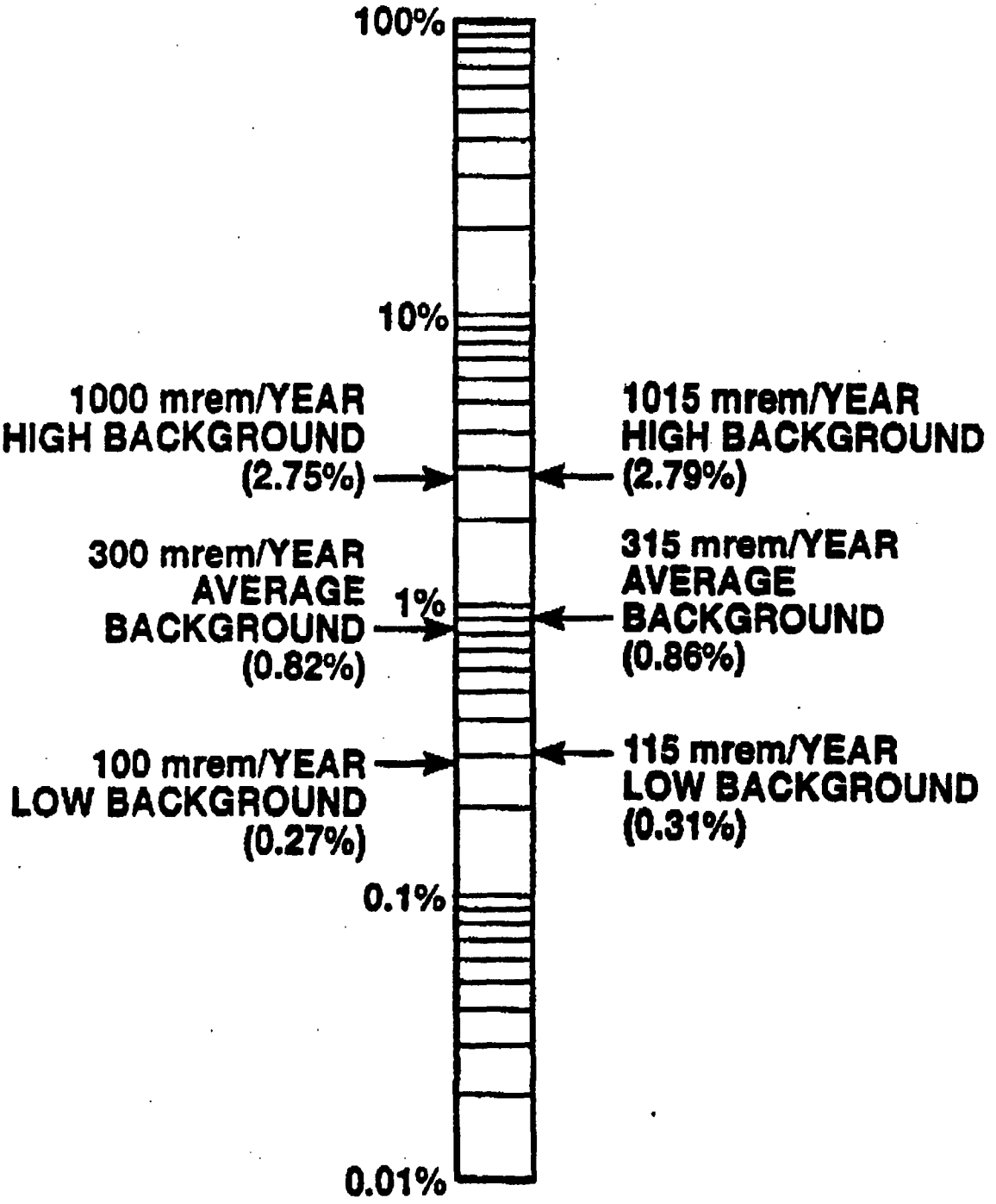


FIGURE 7

ESTIMATED COSTS OF RADIATION MEASUREMENTS

METHOD	COST PER SAMPLE
ALPHA SPECTROMETRY	$300-1000
BETA ANALYSIS	$50-750
EXTERNAL GAMMA EXPOSURE SURVEY	$50
EXTERNAL GAMMA TLD MEASUREMENT	$20
GAMMA SPECTROMETRY	$100-300
RADON MEASUREMENT	$10-20
SOIL SAMPLE COLLECTION	$100-200
SOIL SAMPLE PROCESSING	$100-400
THERMAL IONIZATION MASS SPECTROMETRY	$1000

FIGURE 8

ESTIMATED COST PER MEASUREMENT OF CESIUM-137 IN SOIL

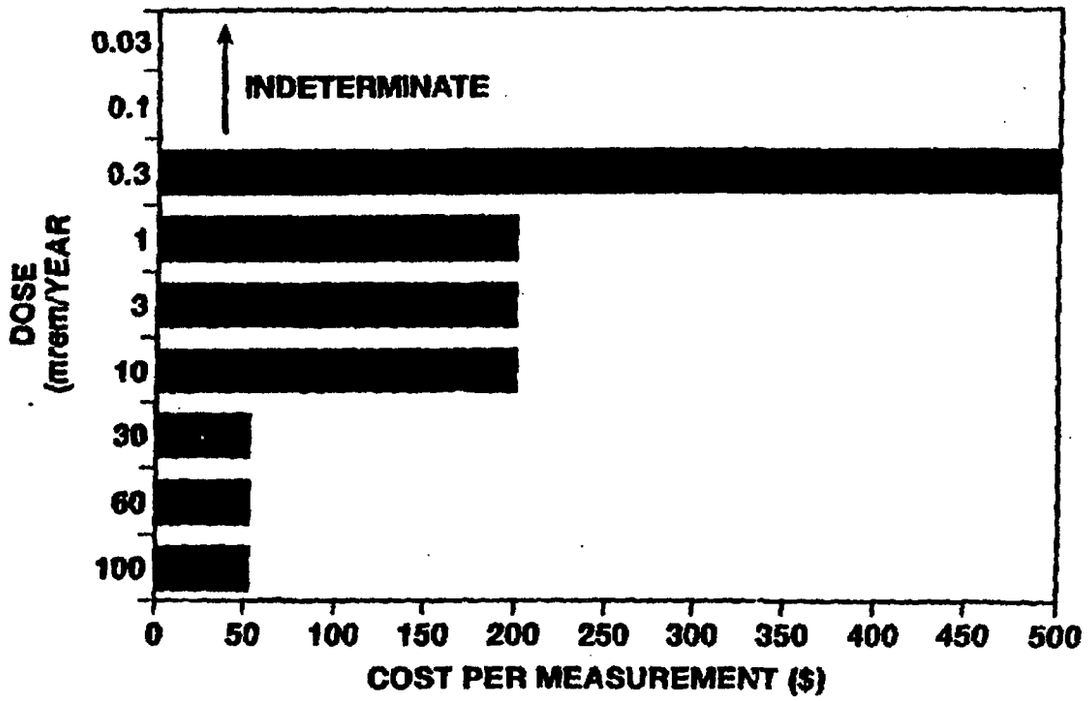


FIGURE 9

Appendix 10

NRC identified a number of other issues that helped in the evaluation of the potential environmental impacts of an ISL facility. These issues include

- **Applicable Statutes, Regulations, and Agencies**. Various statutes, regulations, and implementing agencies at the federal, state, tribal, and local levels that have a role in regulating ISL facilities are identified and discussed.

- **Waste Management**. Potential impacts from the generation, handling, treatment, and final disposal of chemical, radiological, and municipal wastes are addressed.

- **Accidents**. Potential accident conditions are assessed in the GEIS. These include consideration of a range of possible accidents and estimation of their consequences, including well field leaks and spills, excursions, processing chemical spills, and ion-exchange resin and yellowcake transportation accidents.

- **Environmental Justice**. Although not required for a GEIS, to facilitate subsequent site-specific analyses, this GEIS provides a first order definition of minority and low income populations. Early consultations will be initiated with some of these populations, and the potential for disproportionately high and adverse impacts from future ISL licensing in the uranium milling regions will be evaluated in the event ISL license applications are submitted.

- **Cumulative Impacts**. The GEIS addresses cumulative impacts from proposed ISL facility construction, operation, groundwater restoration, and decommissioning on all aspects of the affected environment, by identifying past, present, and reasonably foreseeable future actions in the uranium milling regions.

- **Monitoring**. The GEIS discusses various monitoring methodologies and techniques used to detect and mitigate the spread of radiological and nonradiological contaminants beyond ISL facility boundaries.

SIGNIFICANCE LEVELS

In the GEIS, NRC has categorized the potential environmental impacts using significance levels. According to the Council on Environmental Quality, the significance of impacts is determined by examining both context and intensity (40 CFR 1508.27). Context is related to the affected region, the affected interests, and the locality, while intensity refers to the severity of the impact, which is based on a number of considerations. In this GEIS, the NRC used the significance levels identified in NUREG–1748:

- SMALL Impact: The environmental effects are not detectable or are so minor that they will neither destabilize nor noticeably alter any important attribute of the resource considered.

- MODERATE Impact: The environmental effects are sufficient to alter noticeably, but not destabilize, important attributes of the resource considered.

- LARGE Impact: The environmental effects are clearly noticeable and are sufficient to destabilize important attributes of the resource considered.

SUMMARY OF IMPACTS

Chapter 4 of the GEIS provides NRC's evaluation of the potential environmental impacts of the construction, operation, aquifer restoration, and decommissioning at an ISL facility in each of the four uranium milling regions. A summary of this evaluation by environmental resource area and phase of the ISL facility lifecycle is provided next.

Land Use Impacts

CONSTRUCTION—Land use impacts could occur from land disturbances (including alterations of ecological cultural or historic resources) and access restrictions (including limitations on other mineral extraction activities, grazing activities, or recreational activities). The potential for land use conflicts could increase in areas with higher percentages of private land ownership and Native American land ownership or in areas with a complex patchwork of land ownership. Land disturbances during construction would be temporary and limited to small areas within permitted boundaries. Well sites, staging areas, and trenches would be reseeded and restored. Unpaved access roads would remain in use until decommissioning. Competing access to mineral rights could be either delayed for the duration of the ISL project or be intermixed with ISL operations (e.g., oil and gas exploration). Changes to land use access including grazing restrictions and impacts on recreational activities would be limited due to the small size of restricted areas, temporary nature of restrictions, and availability of other land for these activities. Ecological, historical, and cultural resources could be affected, but would be protected by careful planning and surveying to help identify resources and avoid or mitigate impacts. For all land use aspects except ecological, historical, and cultural resources, the potential impacts would be SMALL. Due to the potential for unidentified resources to be altered or destroyed during excavation, drilling, and grading, the potential impacts to ecological, historical, or cultural resources would be SMALL to LARGE, depending on local conditions.

OPERATION—The types of land use impacts for operational activities would be similar to construction impacts regarding access restrictions because the infrastructure would be in place. Additional land disturbances would not occur from conducting operational activities. Because access restriction and land disturbance related impacts would be similar to, or less than, those for construction, the overall potential impacts to land use from operational activities would be SMALL.

AQUIFER RESTORATION—Due to the use of the same infrastructure, land use impacts would be similar to operations during aquifer restoration, although some operational activities would diminish—SMALL.

DECOMMISSIONING—Land use impacts would be similar to those described for construction with a temporary increase in land-disturbing activities for dismantling, removing, and disposing of facilities, equipment, and excavated contaminated soils. Reclamation of land to preexisting conditions and uses would help mitigate potential impacts—SMALL to MODERATE during decommissioning, and SMALL once decommissioning is completed.

Transportation Impacts

CONSTRUCTION—Low magnitude traffic generated by ISL construction relative to local traffic counts would not significantly increase traffic or accidents on many of the roads in the region. Existing low traffic roads could be moderately impacted by the additional worker commuting traffic during periods of peak employment. This impact would be expected to be more pronounced in areas with relatively lower traffic counts. Moderate dust, noise, and incidental

wildlife or livestock kill impacts would be possible on, or near, site access roads (dust in particular for unpaved access roads)—SMALL to MODERATE.

OPERATION—Low magnitude traffic relative to local traffic counts on most roads would not significantly increase traffic or accidents. Existing low traffic roads could be moderately impacted by commuting traffic during periods of peak employment including dust, noise, and possible incidental wildlife or livestock kill impacts on or near site access roads. High consequences would be possible for a severe accident involving transportation of hazardous chemicals in a populated area. However, the probability of such accidents occurring would be low owing to the small number of shipments, comprehensive regulatory controls, and use of best management practices. For radioactive material shipments (yellowcake product, ion-exchange resins, waste materials), compliance with transportation regulations would limit radiological risk for normal operations. Low radiological risk is estimated for accident conditions. Emergency response protocols would help mitigate long-term consequences of severe accidents involving release of uranium—SMALL to MODERATE.

AQUIFER RESTORATION—The magnitude of transportation activities would be lower than for construction and operations, with the exception of workforce commuting, which could have moderate impacts on, or in the vicinity of, existing low traffic roads—SMALL to MODERATE.

DECOMMISSIONING—The types of transportation activities, and therefore the types of impacts, would be similar to those discussed for construction and operations, except the magnitude of transportation activities (e.g., number and types of waste and supply shipments, no yellowcake shipments) from decommissioning could be lower than for operations. Accident risks would be bounded by the operations yellowcake transportation risk estimates—SMALL.

Geology and Soils Impacts

CONSTRUCTION—Disturbance to soil would occur from construction (clearing, excavation, drilling, trenching, road construction); however, such disturbances would be expected to be temporary, disturbed areas would be small (approximately 15 percent of the total site area), and potential impacts would be mitigated by using best management practices. A large portion of the well fields, trenches, and access roads would be restored and reseeded after construction. Excavated soils would be stockpiled, seeded, and stored onsite until needed for reclamation fill. No impacts to subsurface geological strata would be likely—SMALL.

OPERATION—Temporary contamination or alteration of soils would be likely from operational leaks and spills and possible from transportation, use of evaporation ponds, or land application of treated waste water. However, detection and response to leaks and spills (e.g., soil cleanup), monitoring of treated waste water, and eventual survey and decommissioning of all potentially impacted soils would limit the magnitude of overall impacts to soils—SMALL.

AQUIFER RESTORATION—Impacts to geology and soils from aquifer restoration activities would be similar to impacts from operations due to use of the same infrastructure and similar activities conducted (e.g., well field operation, transfer activities, liquid effluent treatment and disposal)—SMALL.

DECOMMISSIONING—Impacts to geology and soils from decommissioning would be similar to impacts from construction. Activities to clean up, recontour, and reclaim disturbed lands during decommissioning would mitigate long-term impacts to soils—SMALL.

Surface Water Impacts

CONSTRUCTION—Impacts to surface waters and related habitats from construction (road crossings, filling, erosion, runoff, spills or leaks of fuels and lubricants for construction equipment) would be mitigated through proper planning, design, construction methods, and best management practices. Some impacts directly related to the construction activities would be temporary and limited to the duration of the construction period. U.S. Army Corps of Engineers permits may be required when filling and crossing of wetlands. Temporary changes to spring and stream flow from grading and changes in topography and natural drainage patterns could be mitigated or restored after the construction phase. Impacts from incidental spills of drilling fluids into local streams could occur, but would be temporary due to the use of mitigation measures. Impacts from roads, parking areas, and buildings on recharge to shallow aquifers would be SMALL, owing to the limited area of impervious surfaces proposed. Impacts from infiltration of drilling fluids into the local aquifer would be localized, small, and temporary—SMALL to MODERATE depending on site-specific characteristics.

OPERATION—Through permitting processes, federal and state agencies regulate the discharge of storm water runoff and the discharge of process water. Impacts from these discharges would be mitigated as licensees would operate within the conditions of their permits. Expansion of facilities or pipelines during operations would generate impacts similar to construction—SMALL to MODERATE depending on site-specific characteristics.

AQUIFER RESTORATION—Impacts from aquifer restoration would be similar to impacts from operations due to use of the same (in-place) infrastructure and similar activities conducted (e.g., well field operation, transfer of fluids, water treatment, storm water runoff)—SMALL to MODERATE depending on site-specific characteristics.

DECOMMISSIONING—Impacts from decommissioning would be similar to impacts from construction. Activities to clean up, recontour, and reclaim disturbed lands during decommissioning would mitigate long-term impacts to surface waters—SMALL to MODERATE depending on site-specific characteristics.

Groundwater Impacts

CONSTRUCTION—Water use impacts would be limited by the small volumes of groundwater used for routine activities such as dust suppression, mixing cements, and drilling support over short and intermittent periods. Contamination of groundwater from construction activities would be mitigated by best management practices—SMALL.

OPERATION—Potential impacts to shallow aquifers can occur from leaks or spills from surface facilities and equipment. Shallow aquifers are important sources of drinking water in some areas of the four uranium milling regions. Potential impacts to the ore-bearing and surrounding aquifers include consumptive water use and degradation of water quality (from normal production activities, off-normal excursion events, and deep well injection disposal practices). Consumptive use impacts from withdrawal of groundwater would occur because approximately 1 to 3 percent of pumped groundwater is not returned to the aquifer (e.g., process bleed). That amount of water lost could be reduced substantially by available treatment methods (e.g., reverse osmosis, brine concentration). Effects of water withdrawal on groundwater would be expected to be SMALL as the ore zone normally occurs in a confined aquifer. Estimated drawdown effects vary depending on site conditions and water treatment technology applied. Excursions of lixiviant and mobilized chemical constituents could occur from failure of well seals or other operational conditions that result in incomplete recovery of lixiviant. Well-seal-related

excursions would be detected by the groundwater monitoring system, and periodic well mechanical integrity testing, and impacts would be expected to be mitigated during operation or aquifer restoration. Other excursions could result in plumes of mobilized uranium and heavy metals extending beyond the mineralization zone. The magnitude of potential impacts from vertical excursions would vary depending on site-specific conditions. To reduce the likelihood and consequences of potential excursions at ISL facilities, NRC requires licensees to take preventative measures prior to starting operations, including well tests, monitoring, and development of procedures that include excursion response measures and reporting requirements. Impacts from the alterations of ore body aquifer chemistry would be SMALL, because the aquifer would (1) be confined, (2) not be a potential drinking water source, and (3) be expected to be restored during the restoration period. Potential environmental impacts to confined deep aquifers below the production aquifers from deep well injection of processing wastes would be addressed by the underground injection permitting process regulated by the states and NRC's approval process—SMALL to LARGE, depending on site-specific conditions.

AQUIFER RESTORATION—Potential impacts would be from consumptive use and potential deep disposal of brine slurries after reverse osmosis, if applicable. The volume of water removed from the aquifer and related impacts would be dependent on site-specific conditions and the type of water treatment technology the facility uses. In some cases, groundwater consumptive use for the aquifer restoration has been reported to be less than groundwater use during the ISL operation, and drawdowns due to aquifer restorations have been smaller than drawdown caused by ISL operations. Potential environmental impacts associated with water consumption during aquifer restorations are determined by (1) the restoration techniques chosen, (2) the volume of water to be used, (3) the severity and extent of the contamination, and (4) the current and future use of the production and surrounding aquifers near the ISL facility or at the regional scale—SMALL to MODERATE, depending on site-specific conditions.

DECOMMISSIONING—Potential impacts from decommissioning would be similar to construction (water use, spills) with an additional potential to mobilize contaminants during demolition and cleanup activities. Contamination of groundwater from decommissioning activities would be mitigated by implementation of an NRC-approved decommissioning plan and use of best management practices—SMALL.

Terrestrial Ecology Impacts

CONSTRUCTION—Potential terrestrial ecology impacts would include the removal of vegetation from the well fields and the milling site, the modification of existing vegetative communities, the loss of sensitive plants and habitats from clearing and grading, and the potential spread of invasive species and noxious weed populations. These impacts would be expected to be temporary because restoration and reseeding occur rapidly after the end of construction. Introduction of invasive species and noxious weeds would be mitigated by restoration and reseeding after construction. Shrub and tree removal and loss would take longer to restore. Construction noise could affect reproductive success of sage-grouse leks by interfering with mating calls. Temporary displacement of some animal species would also occur. Critical wintering and year-long ranges are important to survival of both big game and sage-grouse. Raptors breeding onsite may be impacted by construction activities or milling operations, depending on the time of year construction occurs. Wildlife habitat fragmentation, temporary displacement of animal species, and direct or indirect mortalities would be possible. Implementation of wildlife surveys and mitigation measures following established guidelines would limit impacts. The magnitude of impacts depends on whether a new facility is being licensed or an existing facility is being extended—SMALL to MODERATE, depending on site-specific habitat conditions.

OPERATION—Habitats could be altered by operations (fencing, traffic, noise), and individual takes could occur due to conflicts between species habitat and operations. Access to crucial wintering habitat and water could be limited by fencing. However, the State of Wyoming Game and Fish Department specifies fencing construction techniques to minimize impediments to big game movement. Migratory birds could be affected by exposure to constituents in evaporation ponds, but perimeter fencing and netting would limit impacts. Temporary contamination or alteration of soils would be likely from operational leaks and spills and possible from transportation or land application of treated waste water. However, detection and response to leaks and spills (e.g., soil cleanup) and eventual survey and decommissioning of all potentially impacted soil limit the magnitude of overall impacts to terrestrial ecology. Mitigation measures such as perimeter fencing, netting, alternative sites, and periodic wildlife surveys would reduce overall impacts—SMALL.

AQUIFER RESTORATION—Impacts include habitat disruption, but existing (in-place) infrastructure would be used during aquifer restoration, with little additional ground disturbance. Migratory birds could be affected by exposure to constituents in evaporation ponds, but perimeter fencing and netting would limit impacts. Contamination of soils could result from leaks and spills and land application of treated waste water. However, detection and response techniques, and eventual survey and decommissioning of all potentially impacted soils, would limit the magnitude of overall impacts to terrestrial ecology. Mitigation measures such as perimeter fencing, netting, and alternative sites would reduce overall impacts—SMALL.

DECOMMISSIONING—During decommissioning and reclamation, there would be a temporary disturbance to land (e.g., excavated soils, buried piping, removal of structures). However, revegetation and recontouring would restore habitat altered during construction and operations. Wildlife would be temporarily displaced, but are expected to return after decommissioning and reclamation are completed and vegetation and habitat are reestablished—SMALL to MODERATE, depending on site-specific conditions.

Aquatic Ecology Impacts

CONSTRUCTION—Clearing and grading activities associated with construction could result in a temporary increase in sediment load in local streams, but aquatic species would recover quickly as sediment load decreases. Clearing of riparian vegetation could affect light and thus the temperature of water. Construction impacts to wetlands would be identified and managed through U.S. Army Corps of Engineers permits, as appropriate. Construction impacts to surface waters and aquatic species would be temporary and mitigated by best management practices—SMALL.

OPERATION—Impacts could result from spills or releases into surface water. Impacts would be minimized by spill prevention, identification, and response programs, and National Pollutant Discharge Elimination System (NPDES) permit requirements—SMALL.

AQUIFER RESTORATION—Activities would use existing (in-place) infrastructure, and impacts could result from spills or releases of untreated groundwater. Impacts would be minimized by spill prevention, identification, and response programs, and NPDES permit requirements—SMALL.

DECOMMISSIONING—Decommissioning and reclamation activities could result in temporary increases in sediment load in local streams, but aquatic species would recover quickly as

sediment load decreases. With completion of decommissioning, revegetation, and recontouring, habitat would be reestablished and impacts would, therefore, be limited—SMALL.

Threatened and Endangered Species Impacts

CONSTRUCTION—Numerous threatened and endangered species and state species of concern are located in the four uranium milling regions. Small fragmentation of habitats would occur, but most species readapt quickly. The magnitude of impact would depend on the size of a new facility or extension to an existing facility and the amount of land disturbance. Inventory of threatened or endangered species would be developed during site-specific reviews to identify unique or special habitats, and Endangered Species Act consultations conducted with the U.S. Fish and Wildlife Service would assist in reducing impacts—SMALL to LARGE—depending on site-specific habitat and presence of threatened or endangered species.

OPERATION—Impacts could result from individual takes due to conflicts with operations. Small fragmentation of habitats would occur, but most species readapt quickly. The magnitude of impact would depend on the size of a new facility or extension to an existing facility and the amount of land disturbance. Impacts could potentially result from spills or permitted effluents, but would be minimized through the use of spill prevention measures, identification and response programs, and NPDES permit requirements. Inventory of threatened or endangered species developed during site-specific reviews would identify unique or special habitats, and Endangered Species Act consultations conducted with the U.S. Fish and Wildlife Service would assist in reducing impacts—SMALL to LARGE—depending on site-specific habitat and presence of threatened or endangered species.

AQUIFER RESTORATION—Impacts could result from individual takes due to conflicts with aquifer restoration activities (equipment, traffic). Existing (in-place) infrastructure would be used during aquifer restoration, so additional land-disturbing activities and habitat fragmentation would not be anticipated. Impacts may result from spills or releases of treated or untreated groundwater, but impacts would be minimized through the use of spill prevention measures, identification and response programs, and NPDES permit requirements. Inventory of threatened or endangered species would be developed during site-specific reviews to identify unique or special habitats, and Endangered Species Act consultations with the U.S. Fish and Wildlife Service would assist in reducing impacts—SMALL.

DECOMMISSIONING—Impacts resulting from individual takes would occur due to conflicts with decommissioning activities (equipment, traffic). Temporary land disturbance would occur as structures are demolished and removed and the ground surface is recontoured. Inventory of threatened or endangered species developed during site-specific environmental review of the decommissioning plan would identify unique or special habitats, and Endangered Species Act consultations with the U.S. Fish and Wildlife Service would assist in reducing impacts. With completion of decommissioning, re-vegetation, and re-contouring, habitat would be reestablished and impacts would, therefore, be limited—SMALL to LARGE.

Air Quality Impacts

CONSTRUCTION—Fugitive dust and combustion (vehicle and diesel equipment) emissions during land-disturbing activities associated with construction would be small, short-term, and reduced through best management practices (e.g., dust suppression). For example, estimated fugitive dust emissions during ISL construction are less than 2 percent of the National Ambient Air Quality Standards (NAAQS) for $PM_{2.5}$ and less than 1 percent for PM_{10}. For NAAQS attainment areas, nonradiological air quality impacts would be SMALL. A Prevention of

Significant Deterioration Class I area exists in only one of the four regions (Wind Cave National Park in the Nebraska-South Dakota-Wyoming Region). More stringent air quality standards would apply to a facility that impacts the air quality of that area. If impacts were initially assessed at a higher significance level, permit requirements would impose conditions or mitigation measures to reduce impacts—SMALL.

OPERATION—Radiological impacts can result from dust releases from drying of lixiviant pipeline spills, radon releases from well system relief valves, resin transfer or elution, and gaseous/particulate emissions from yellowcake dryers. Only small amounts of low dose materials would be expected to be released based on operational controls and rapid response to spills. Required spill prevention, control, and response procedures would be used to minimize impacts from spills. HEPA filters and vacuum dryer designs reduce particulate emissions from operations, and ventilation reduces radon buildup during operations. Compliance with the NRC-required radiation monitoring program would ensure releases are within regulatory limits. Other potential nonradiological emissions during operations include fugitive dust and fuel from equipment, maintenance, transport trucks, and other vehicles. For NAAQS attainment areas, nonradiological air quality impacts would be SMALL. A Prevention of Significant Deterioration Class I area is located in the Nebraska-South Dakota-Wyoming Region (Wind Cave National Park). More stringent air quality standards would apply to a facility that impacts the air quality of that area. If impacts were initially assessed at a higher significance level, permit requirements would impose conditions or mitigation measures to reduce impacts—SMALL.

AQUIFER RESTORATION—Because the same infrastructure is used, air quality impacts are expected to be similar to, or less than, those during operations. For NAAQS attainment areas, nonradiological air quality impacts would be SMALL. Where a Prevention of Significant Deterioration Class I area exists, such as the Wind Cave National Park in the Nebraska-South Dakota-Wyoming Region, more stringent air quality standards would apply to a facility that impacts the air quality. If impacts were initially assessed at a higher significance level, permit requirements would impose conditions or mitigation measures to reduce impacts—SMALL.

DECOMMISSIONING—Fugitive dust, vehicle, and diesel emissions during land-disturbing activities associated with decommissioning would be similar to, or less than, those associated with construction, would be short-term, and would be reduced through best management practices (e.g., dust suppression). Potential impacts would decrease as decommissioning and reclamation of disturbed areas are completed. For NAAQS attainment areas, nonradiological air quality impacts would be SMALL. However, where a Prevention of Significant Deterioration Class I area exists (Wind Cave National Park in the Nebraska-South Dakota-Wyoming Region), more stringent air quality standards would apply to a facility that impacts the air quality of that area. If impacts were initially assessed at a higher significance level, permit requirements would impose conditions or mitigation measures to reduce impacts—SMALL.

Noise Impacts

CONSTRUCTION—Noise generated during construction would be noticeable in proximity to operating equipment, but would be temporary (typically daytime only). Administrative and engineering controls would be used to maintain noise levels in work areas below Occupational Health and Safety Administration (OSHA) regulatory limits and mitigated by use of personal hearing protection. Traffic noise during construction (commuting workers, truck shipments to and from the facility, and construction equipment such as trucks, bulldozers, and compressors) would be localized, and limited to highways in the vicinity of the site, access roads within the site, and roads in the well fields. Relative increases in traffic levels would be SMALL for the

larger roads, but may be MODERATE for lightly traveled rural roads through smaller communities. Noise may also adversely affect wildlife habitat and reproductive success in the immediate vicinity of construction activities. Noise levels decrease with distance, and at distances more than about 300 m [1,000 ft], ambient noise levels would return to background. Wildlife avoid construction areas because of noise and human activity. Generally, the uranium districts are located more than 300 m [1,000 ft] from the closest community. As a result, noise impacts would be SMALL to MODERATE.

OPERATION—Noise-generating activities in the central uranium processing facility would be indoors, reducing offsite sound levels. Well field equipment (e.g., pumps, compressors) would be contained within structures (e.g., header houses, satellite facilities), also reducing sound levels to offsite receptors. Administrative and engineering controls would be used to maintain noise levels in work areas below OSHA regulatory limits and mitigated by use of personal hearing protection. Traffic noise from commuting workers, truck shipments to and from the facility, and facility equipment would be expected to be localized, limited to highways in the vicinity of the site, access roads within the site, and roads in well fields. Relative increases in traffic levels would be SMALL for the larger roads, but may be MODERATE for lightly traveled rural roads through smaller communities. Most noise would be generated indoors and mitigated by regulatory compliance and best management practices. Noise from trucks and other vehicles is typically of short duration. Also, noise usually is not discernable to offsite receptors at distances of more than 300 m [1,000 ft.] Generally, the uranium districts are located more than 300 m [1,000 ft] from the closest community—SMALL to MODERATE.

AQUIFER RESTORATION—Noise generation is expected to be less than during construction and operations. Pumps and other well field equipment contained in buildings reduce sound levels to offsite receptors. Existing operational infrastructure would be used, and traffic levels would be expected to be less than those during construction and operations. There are additional sensitive areas that should be considered within some of the regions, but because of decreasing noise levels with distance, aquifer restoration activities would have only SMALL and temporary noise impacts for residences, communities, or sensitive areas, especially those located more than about 300 m [1,000 ft] from specific noise-generating activities. Noise usually is not discernable to offsite receptors at distances more than 300 m [1,000 ft]. Generally, the uranium districts are located more than 300 m [1,000 ft] from the closest community—SMALL to MODERATE.

DECOMMISSIONING—Noise generated during decommissioning would be noticeable only in proximity to equipment and temporary (typically daytime only). Administrative and engineering controls would be used to maintain noise levels in work areas below OSHA regulatory limits and mitigated by use of personal hearing protection. Noise levels during decommissioning would be less than during construction and would diminish as less and less equipment is used and truck traffic is reduced. Noise usually is not discernable to offsite receptors at distances more than 300 m [1,000 ft]. Generally, the uranium districts are located more than 300 m [1,000 ft] from the closest community—SMALL to MODERATE.

Historical and Cultural Resources Impacts

CONSTRUCTION—Potential impacts during ISL facility construction could include loss of, or damage and temporary restrictions on access to, historical, cultural, and archaeological resources. The eligibility evaluation of cultural resources for listing in the National Register of Historic Places (NRHP) under criteria in 36 CFR 60.4(a)–(d) and/or as Traditional Cultural Properties (TCP) would be conducted as part of the site-specific review and NRC licensing procedures undertaken during the NEPA review process. The evaluation of impacts to any

historic properties designated as TCPs and tribal consultations regarding cultural resources and TCPs also occurs during the site-specific licensing application and review process. To determine whether significant cultural resources would be avoided or mitigated, consultations with State Historic Preservation Offices (SHPO), other government agencies (e.g., U.S. Fish and Wildlife Service and State Environmental Departments), and Native American Tribes (the THPO) occur as part of the site-specific review. Additionally, as needed, the NRC license applicant would be required, under conditions in its NRC license, to adhere to procedures regarding the discovery of previously undocumented cultural resources during initial construction. These procedures typically require the licensee to stop work and to notify the appropriate federal, tribal, and state agencies with regard to mitigation measures—SMALL or MODERATE to LARGE depending on site-specific conditions.

OPERATION—Because less land disturbance occurs during the operations phase, potential impacts to historical, cultural, and archaeological resources would be less than during construction. Conditions in the NRC license requiring adherence to procedures regarding the discovery of previously undocumented cultural resources would apply during operation. These procedures typically require the licensee to stop work and to notify the appropriate federal, tribal, and state agencies with regard to mitigation measures—SMALL, depending on site-specific conditions.

AQUIFER RESTORATION—Because less land disturbance occurs during the aquifer restoration phase, potential impacts to historical, cultural, and archaeological resources would be less than those during construction. Conditions in the NRC license requiring adherence to procedures regarding the discovery of previously undocumented cultural resources would apply during aquifer restoration. These procedures typically require the licensee to stop work and to notify the appropriate federal, tribal, and state agencies with regard to mitigation measures—SMALL, depending on site-specific conditions.

DECOMMISSIONING—Because less land disturbance occurs during the decommissioning phase and because decommissioning and reclamation activities would be focused on previously disturbed areas, potential impacts to historical, cultural, and archaeological resources would be less than during construction. Conditions in the NRC license requiring adherence to procedures regarding the discovery of previously undocumented cultural resources would apply during decommissioning and reclamation. These procedures typically require the licensee to stop work and to notify the appropriate federal, tribal, and state agencies with regard to mitigation measures—SMALL, depending on site-specific conditions.

Visual and Scenic Impacts

CONSTRUCTION—Visual impacts result from equipment (drill rig masts, cranes), dust/diesel emissions from construction equipment, and hillside and roadside cuts. Most of the four uranium milling regions are classified as Visual Resource Management (VRM) Class II through IV by the U.S. Bureau of Land Management. A number of VRM Class II areas surround national monuments (El Morro and El Malpais), the Chaco Culture National Historic Park, and sensitive areas managed within the Mount Taylor district in the Northwestern New Mexico Uranium Milling District and would have the greatest potential for impacts to visual resources. Most of these areas, however, are located away from potential ISL facilities at distances greater than 16 km [10 mi]. Most potential facilities are located in VRM Class III and IV areas. The general visual and scenic impacts associated with ISL facility construction would be temporary and SMALL, but from a Native American perspective, any construction activities would likely result in adverse impacts to the landscape, particularly for facilities located in areas within view of tribal lands and areas of special significance such as Mount Taylor. As previously discussed,

a Prevention of Significant Deterioration Class I area (Wind Cave National Park) is located in the Nebraska-South Dakota-Wyoming Uranium Milling Region. Prevention of Significant Deterioration Class I areas require more stringent air quality standards that can affect visual impacts. Nevertheless, most potential visual impacts during construction would be temporary as equipment is moved and would be mitigated by best management practices (e.g., dust suppression). Because these sites are in sparsely populated areas and there is generally rolling topography of the region, most visual impacts during construction would not be visible from more than about 1 km [0.6 mi]. The visual impacts associated with ISL construction would be consistent with the predominant VRM Class III and IV—SMALL.

OPERATION—Visual impacts during operations would be less than those associated with construction. Most of the well field surface infrastructure has a low profile, and most piping and cables would be buried. The tallest structures include the central uranium processing facility {10 m [30 ft]} and power lines {6 m [20 ft]}. Because these sites are in sparsely populated areas and there is generally rolling topography of the regions, most visual impacts during operations would not be visible from more than about 1 km [0.6 mi]. Irregular layout of well field surface structures such as wellhead protection and header houses would further reduce visual contrast. Best management practices, and design (e.g., painting buildings) and landscaping techniques would be used to mitigate potential visual impact. The uranium districts in the four regions are all located more than 16 km [10 mi] from the closest VRM Class II region, and the visual impacts associated with ISL construction would be consistent with the predominant VRM Class III and IV—SMALL.

AQUIFER RESTORATION—Aquifer restoration activities would use in-place infrastructure. As a result, potential visual impacts would be the same as, or less than, those during operations—SMALL.

DECOMMISSIONING—Because similar equipment would be used and activities conducted, potential visual impacts during decommissioning would be the same as, or less than, those during construction. Most potential visual impacts during decommissioning would be temporary as equipment is moved and would be mitigated by best management practices (e.g., dust suppression). Visual impacts would be low, because these sites are in sparsely populated areas, and impacts would diminish as decommissioning activities decrease. An approved site reclamation plan is required prior to license termination, with the goal of returning the landscape to preconstruction conditions (predominantly VRM Class III and IV). Some roadside cuts and hill slope modifications, however, may persist beyond decommissioning and reclamation—SMALL.

Socioeconomic Impacts

CONSTRUCTION—Potential impacts to socioeconomics would result predominantly from employment at an ISL facility and demands on the existing public and social services, tourism/recreation, housing, infrastructure (schools, utilities), and the local work force. Total peak employment would be about 200 people, including company employees and local contractors, depending on timing of construction with other stages of the ISL lifecycle. During construction of surface facilities and well fields, the general practice would be to use local contractors (drillers, construction), as available. A local multiplier of 0.7 (U.S. Bureau of the Census) is used to indicate how many ancillary jobs could be created (in this case about 140). For example, local building materials and building supplies would be used to the extent practical. Most employees would live in larger communities with access to more services. Some construction employees, however, would commute from outside the county to the ISL facility, and skilled employees (e.g., engineers, accountants, managers) would come from outside the

local work force. Some of these employees would temporarily relocate to the project area and contribute to the local economy through purchasing goods and services and taxes. Because of the small relative size of the ISL workforce, net impacts would be SMALL to MODERATE.

OPERATION—Employment levels for ISL facility operations would be less than those for construction, with total peak employment depending on timing and overlap with other stages of the ISL lifecycle. Use of local contract workers and local building materials would diminish, because drilling and facility construction would diminish. Revenues would be generated from federal, state, and local taxes on the facility and the uranium produced. Employment types would be similar to construction, but the socioeconomic impacts would be less due to fewer employees—SMALL to MODERATE.

AQUIFER RESTORATION—In-place infrastructure would be used for aquifer restoration, and employment levels would be similar to those for operations—SMALL to MODERATE.

DECOMMISSIONING—A skill set similar to the construction workforce would be involved in dismantling surface structures, removing pumps, plugging and abandoning wells, and reclaiming/recontouring the ground surface. Employment levels and use of local contractor support during decommissioning would be similar to those required for construction. Employment would be temporary, however, as decommissioning activities are short in duration. Because of similar employment levels, other socioeconomic impacts would be similar to construction—SMALL to MODERATE.

Public and Occupational Health and Safety Impacts

CONSTRUCTION—Worker safety would be addressed by standard construction safety practices. Fugitive dust would result from construction activities and vehicle traffic, but would likely be of short duration and would not result in a radiological dose. Diesel emissions would also be of short duration and readily dispersed into the atmosphere—SMALL to MODERATE.

OPERATION—Potential occupational radiological impacts from normal operations would result from (1) exposure to radon gas from the well field, (2) ion-exchange resin transfer operations, and (3) venting during processing activities. Workers would also be exposed to airborne uranium particulates from dryer operations and maintenance activities. Potential public exposures to radiation could occur from the same radon releases and uranium particulate releases (i.e., from facilities without vacuum dryer technology). Both worker and public radiological exposures are addressed in NRC regulations at 10 CFR Part 20, which require licensees to implement an NRC-approved radiation protection program. (Measured and calculated doses for workers and the public are commonly only a fraction of regulated limits.) Nonradiological worker safety matters are addressed through commonly applied occupational health and safety regulations and practices. Radiological accident risks could involve processing equipment failures leading to yellowcake slurry spills, or radon gas or uranium particulate releases. Consequences of accidents to workers and the public are generally low, with the exception of a dryer explosion which could result in worker dose above NRC limits. The likelihood of such an accident would be low, and therefore the risk would also be low. Potential nonradiological accidents impacts include high consequence chemical release events (e.g., ammonia) for both workers and nearby populations. The likelihood, however, of such release events would be low based on historical operating experience at NRC-licensed facilities, primarily due to operators following commonly applied chemical safety and handling protocols—SMALL to MODERATE.

AQUIFER RESTORATION—Activities during aquifer restoration overlap with similar activities during operations (e.g., operation of well fields, waste water treatment and disposal). The resultant impacts on public and occupational health and safety would be bound by operational impacts. The reduction of some operational activities (e.g., yellowcake production and drying, remote ion exchange) will limit the relative magnitude of potential worker and public health and safety hazards—SMALL.

DECOMMISSIONING—Worker and public health and safety would be addressed in a NRC-required decommissioning plan. This plan details how a 10 CFR Part 20 compliant radiation safety program would be implemented during decommissioning, how ensuring the safety of workers and the public would be maintained, and how applicable safety regulations would be complied with—SMALL.

Waste Management Impacts

CONSTRUCTION—Relatively small-scale construction activities (Section 2.3) and incremental well field development at ISL facilities would generate low volumes of construction waste—SMALL.

OPERATION—Operational wastes primarily result from liquid waste streams including process bleed, flushing of depleted eluant to limit impurities, resin transfer wash, filter washing, uranium precipitation process wastes (brine), and plant wash down water. State permit actions, NRC license conditions, and NRC inspections ensure the proper practices would be used to comply with safety requirements to protect workers and the public. Waste treatments such as reverse osmosis and radium settling would be used to segregate wastes and minimize disposal volumes. Potential impacts from surface discharge and deep well injection would be limited by the conditions specified in the applicable state permit. NRC regulations address constructing, operating, and monitoring for leakage of evaporation ponds used to store and reduce volumes of liquid wastes. Potential impacts from land application of treated wastewater would be addressed by NRC review of site-specific conditions prior to approval and routine monitoring in decommissioning surveys. Offsite waste disposal impacts would be SMALL for radioactive wastes as a result of required preoperational disposal agreements. Impacts for hazardous and municipal waste would also be SMALL due to the volume of wastes generated. For remote areas with limited available disposal capacity, such wastes may need to be shipped greater distances to facilities that have capacity; however, the volume of wastes generated and magnitude of such shipments are estimated to be low—SMALL.

AQUIFER RESTORATION—Waste management activities during aquifer restoration would use the same treatment and disposal options implemented for operations. Therefore, impacts associated with aquifer restoration would be similar to operational impacts. While the amount of wastewater generated during aquifer restoration would be dependent on site-specific conditions, the potential exists for additional wastewater volume and associated treatment wastes during the restoration period. However, this would be offset to some degree by the reduction in production capacity from the removal of a well field. NRC review of future ISL facility applications would verify that sufficient water treatment and disposal capacity (and the associated agreement for disposal of byproduct material) are addressed. As a result, waste management impacts from aquifer restoration would be SMALL.

DECOMMISSIONING—Radioactive wastes from decommissioning ISL facilities (including contaminated excavated soil, evaporation pond bottoms, process equipment) would be disposed of as byproduct material at an NRC-licensed facility. A preoperational agreement with a licensed disposal facility to accept radioactive wastes ensures sufficient disposal capacity

would be available for byproduct wastes generated by decommissioning activities. Safe handling, storage, and disposal of decommissioning wastes would be addressed in a required decommissioning plan for NRC review prior to starting decommissioning activities. Such a plan would detail how a 10 CFR Part 20 compliant radiation safety program would be implemented during decommissioning to ensure the safety of workers and the public and compliance with applicable safety regulations. Overall, volumes of decommissioning radioactive, chemical, and solid wastes would be SMALL.