LANL-MISC

University of California
Los Alamos National Laboratory

Third Community Environmental Meeting

An Update on Brain Tumor and Thyroid Cancer Rates in Los Alamos County

Wednesday, November 5, 1997, 7:00–9:00 P.M.
Fuller Lodge, Los Alamos, NM

John ✓
Jmarie ✓
Ralph ✓
Scott ✓
Dave ✓
Tom ✓
Tim ✓
Chris ✓
Mike
Bruce ✓

AGENDA

7:00	Introduction	Joan McIver Gibson
7:05	Welcome	Dennis J. Erickson
7:10	Review of the Los Alamos Cancer Rate Study	C. Mack Sewell
7:30	Recent Data on Brain Tumor and Thyroid Cancer Rates in Los Alamos County	Charles R. Key, M.D.
7:50	Break	
8:00	Panel/Public Discussion: Should Los Alamos Residents Be Concerned?	Joan McIver Gibson, moderator
9:00	Adjourn	

Panel participants:*

Joan McIver Gibson, Director, Health Sciences Ethics Program, University of New Mexico
Charles Key, M.D., Director, New Mexico Tumor Registry
Mack Sewell, director, Division of Epidemiology, New Mexico Department of Health
Kenneth Silver, gradute student, Boston University School of Public Health
Helen Stanbro,[1,2] resident, Los Alamos Resident
John Stroud,[1] board member, Concerned Citizens for Nuclear Safety
Laurie Wiggs,[1] epidemiologist, Los Alamos National Laboratory

[1] *Member of the Steering Committee, Los Alamos Cancer Rate Study (LACRS)*
[2] *Member of the Thyroid Cancer Technical Steering Subcommittee of the LACRS*

*Biographies appear on reverse side

About the Panelists

Joan McIver Gibson received an A.B. in philosophy from Mount Holyoke College and an M.A. and Ph.D. in philososphy from the University of California at San Diego. She is director of the Health Sciences Ethics Program at UNM and medical ethicist for the St. Joseph Healthcare System in Albuquerque. From 1971 to 1986, she was associate professor of philosophy at the University of Albuquerque; from 1986 to 1994, she was senior program director at the UNM Institute of Public Law. Her areas of expertise are ethics committees in health care institutions, issues surrounding life support treatment, applied ethics in industry and business, and mediation applied to ethical issues. Dr. Gibson, who trains judges around the country in issues of bioethics, was a member of the Clinton administration's Health Policy Task Force (Ethics Working Group) and serves on the ES&H Panel of the University of California President's Council on the National Laboratories.

Charles R. Key earned his M.D. in pathology and Ph.D. in medical sciences-pathology at the University of Oklahoma. He is currently director of the New Mexico Tumor Registry (NMTR) at UNM. Following graduate studies and residency in anatomic and clinical pathology at the University of Oklahoma Medical Center, he served for five years in the US Public Health Service, including three years at the Atomic Bomb Casualty Commission (now Radiation Effects Research Foundation) in Hiroshima, Japan. Dr. Key joined the Department of Pathology at the UNM medical school in 1969. Dr. Key's research has focused on the operation and utilization of the NMTR for descriptive studies of the different patterns of cancer (incidence, extent of disease at diagnosis, choice of treatment, and outcome) and their changes over time among American Indians, Hispanics and non-Hispanic Whites. During 1992–94, Dr. Key served as Acting Chairman of Pathology, and in 1995–96, he was interim director of the UNM Cancer Research and Treatment Center.

C. Mack Sewell received the Dr.P.H. in public health from the University of Texas School of Public Health, Houston, an M.S. in microbiology from Colorado State University, and a B.S. in biology and chemistry from New Mexico State University. Dr. Sewell joined the NM Health and Environment Department in 1984 as an epidemiologist and is now State Epidemiologist and director of the Division of Epidemiology, Evaluation and Planning at the NM Department of Health. He has been an adjunct professor at the University of Texas School of Public Health and is presently a clinical associate at the Department of Family, Community and Emergency Medicine at the UNM School of Medicine.

Ken Silver is a doctoral candidate in environmental health at the Boston University School of Public Health. He received a B.S. in chemistry from the University of Massachusetts and an S.M. in environmental health from Harvard. As a doctoral candidate supported under a cooperative agreement between Boston University and the Agency for Toxic Substances and Disease Registry (ATSDR) to assist with public health assessments at Department of Energy sites, he returned to Harvard in 1993 for course work in radiation biology. In mid-1994 Mr. Silver began work in support of ATSDR's public health assessment of Los Alamos National Laboratory and decided to make historical emissions from the Laboratory a centerpiece of his dissertation.

Helen Stanbro holds an M.Ph. in genetics from George Washington University in Washington, D.C. She has worked for 17 years as a medical information specialist for the National Library of Medicine on data bases such as CANCERPROJ and MEDLINE. She was a community member of several groups that investigated health issues in Los Alamos: the Working Group to Address Los Alamos Community Health Concerns, the Steering Committee for the Los Alamos Cancer Rate Study, and the Thyroid Cancer Technical Steering Sub-Committee. She has lived in Los Alamos since 1989.

John Stroud received a B.S. in physics from Bethany College and a J.D. from Capital University in Columbus, Ohio. He was in private law practice for about 20 years and now works on water right adjudication, primarily on Native American water rights issues, for the NM State Engineer office. He is a member of the board of Concerned Citizens for Nuclear Safety and was a member of the Steering Committee for the Los Alamos Cancer Rate Study.

Laurie Wiggs received a M.P.H. degree and a Ph.D. in epidemiology with a minor in biostatistics from the University of Oklahoma School of Public Health. She has 18 years experience as an environmental epidemiologist. She serves as epidemiology team leader in the Laboratory's Occupational Medicine group and is also an adjunct professor of biostatistics and epidemiology at the University of Oklahoma. Dr. Wiggs directed the National Plutonium Workers Study and has served on many committees and panels, such as the Study Group for the Combined Analyses of Cancer Mortality among Radiation Workers of the World Health Organization, the Working Group to Address Los Alamos Community Health Concerns, and the Steering Committee of the Los Alamos Cancer Rate Study.

MORTALITY DATA

TABLE 8: NUMBER OF DEATHS FROM ALL CAUSES AND CRUDE DEATH RATES PER 1,000 POPULATION

YEAR	Los Alamos County NUMBER	Los Alamos County RATE	New Mexico RATE	United States RATE
1995	86	4.6	7.4	8.8
1994	96	5.2	7.3	8.8
1993	93	5.1	7.2	8.8
1992	71	3.9	7.0	8.5
1991	103	5.8	7.3	8.6
1990	98	5.4	7.0	8.6
1980	54	3.1	6.9	8.8

GRAPH 9: STANDARD MORTALITY RATIOS 1992-1994

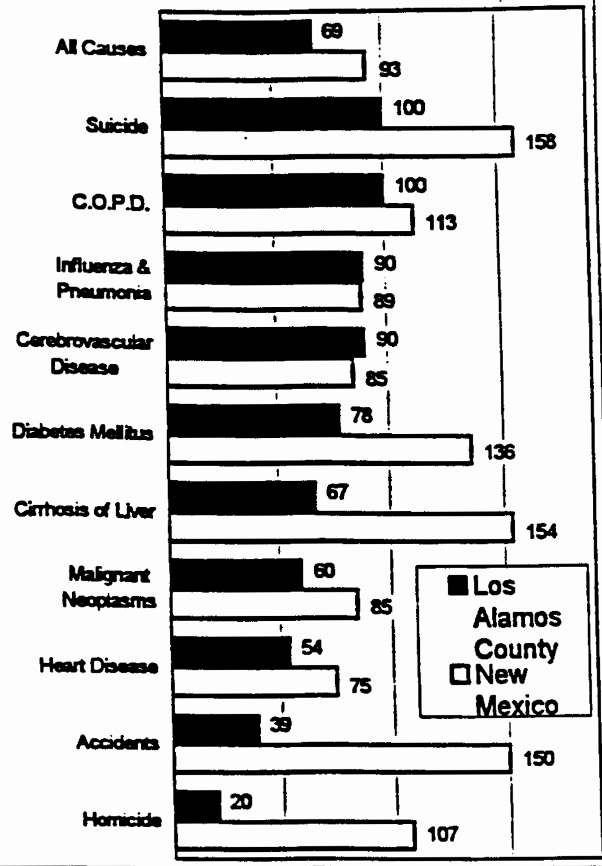
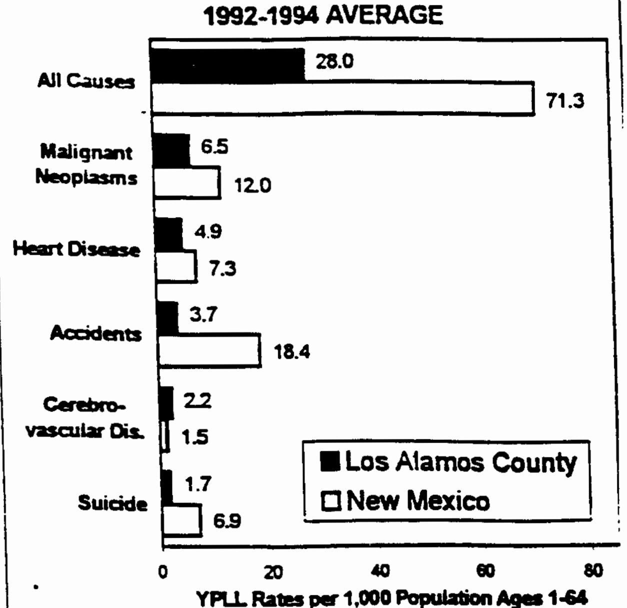


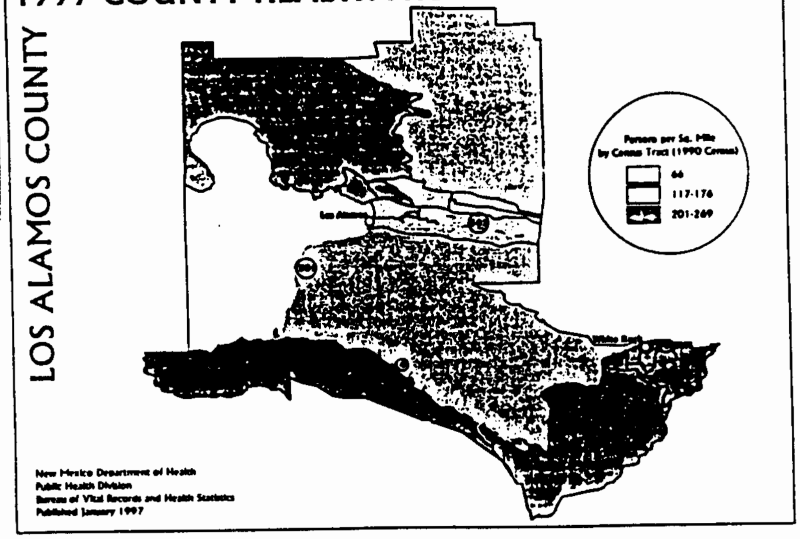
TABLE 9: 1992-1994 AGGREGATE NUMBER OF RESIDENT DEATHS BY SELECTED CAUSES

Cause of Death	Los Alamos County	New Mexico
All Causes	260	34,993
Heart Disease	61	8,964
Malignant Neoplasms	60	7,652
Accidents	7	2,426
Cerebrovascular Disease	19	2,014
C.O.P.D.	16	1,887
Influenza & Pneumonia	9	1,155
Suicide	7	894
Diabetes Mellitus	7	1,208
Cirrhosis of Liver	4	682
Homicide	1	521

GRAPH 10: YEARS OF POTENTIAL LIFE LOST (YPLL) SELECTED CAUSES: 1992-1994 AVERAGE



1997 COUNTY HEALTH PROFILE



STANDARD MORTALITY RATIO (SMR)—The ratio of the observed deaths to the expected deaths times 100. number of expected deaths is derived using the national mortality as a standard and are age/sex adjuste

YEARS OF POTENTIAL LIFE LOST (YPLL)—The measure of the number of years of potential life lost by each death occurring before a predetermined end point (the average expected lifetime). Data presented specific to deaths of persons dying in the 1-64 age group.

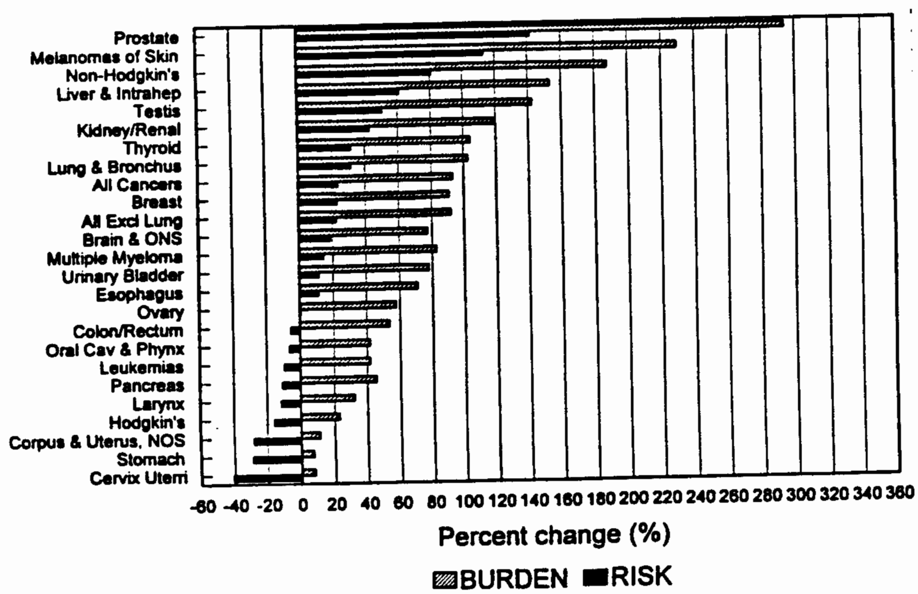
Los Alamos Cancer Update
November 5, 1997

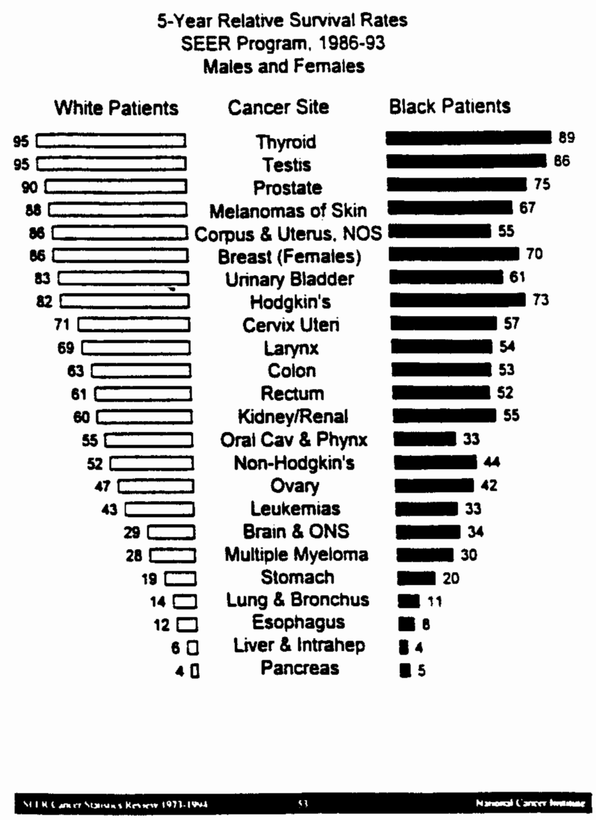
All Cancers	BURDEN *estimated number of cases, 1997*		RISK *age-adjusted rate, 1990-94** *(per 100,000 per yr)*		PROGNOSIS *5-yr relative survival, 1986-93*
	Diagnoses	Deaths	Incidence	Mortality	
U.S. (total)	1,257,000	560,000	409.0	172.3	57.9%
Male	661,200	294,100	510.2	217.9	54.6%
Female	596,600	265,900	346.3	141.9	61.0%
N.M. (total)	*6,000*	*2,800*	346.2	145.8	59.5%
Male	*3,200*	*1,500*	422.4	181.1	57.8%
Female	*2,800*	*1,300*	290.0	120.1	61.0%
Los Alamos	85	21	451	~104	73%
Male	44	12	512	(SMR=	70%
Female	41	9	410	60)	78%

Sources: SEER Cancer Statitics Review, 1973-94 (NIH Publication No. 97-2789), National Cancer Institute, see also: http://www-seer.ims.nci.nih.gov; Los Alamos 1997 County Health Profile (NM Dept of Health); and New Mexico Tumor Registry

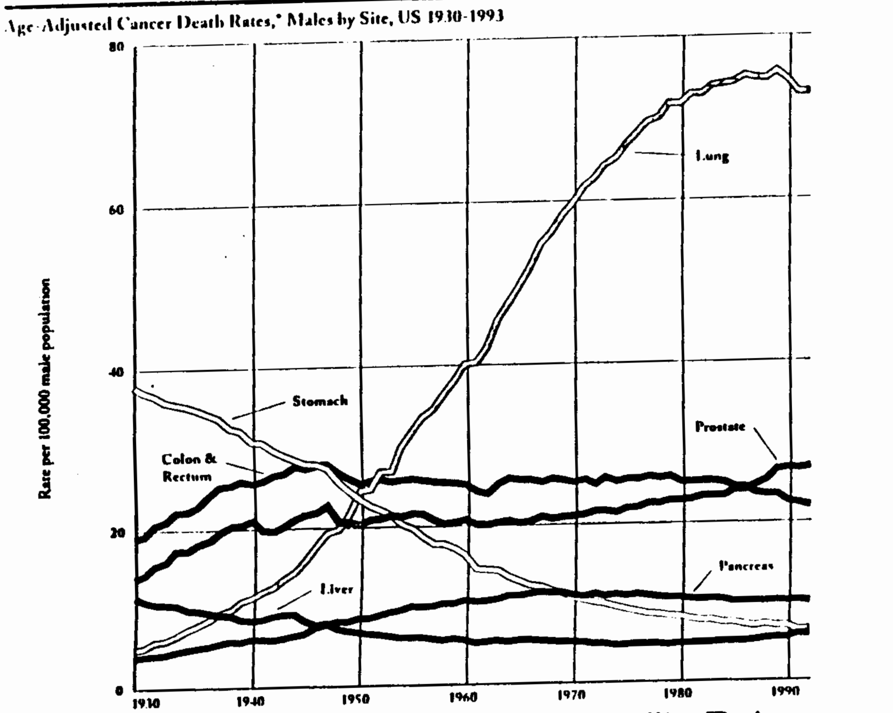
**1970 U.S. population standard*

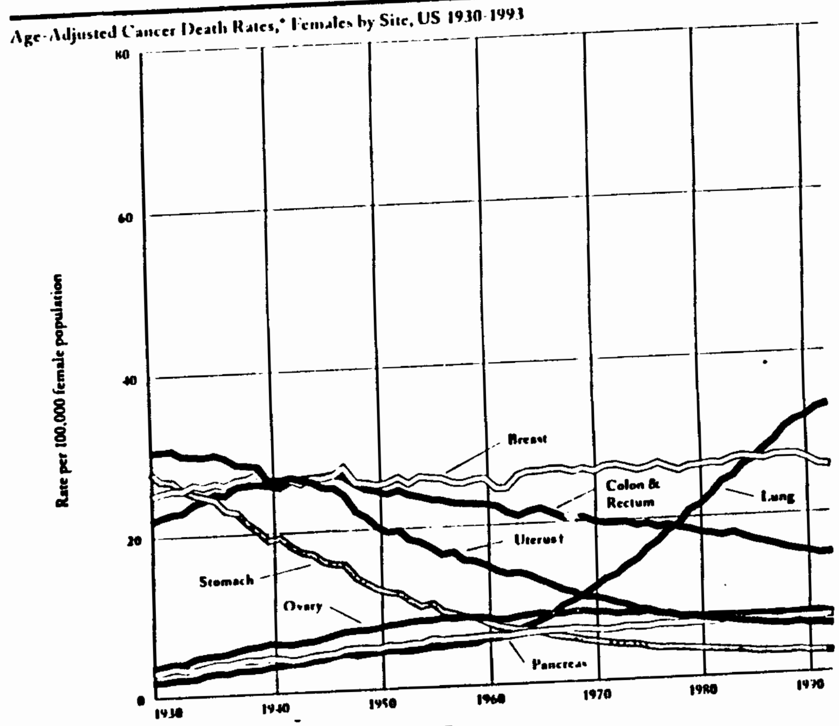
Incidence Percent Change, 1973 to 1994
Numbers (burden) vs. Rates (risk)
All Ages





U S incidence estimates based on SEER age-specific rates applied to U S population



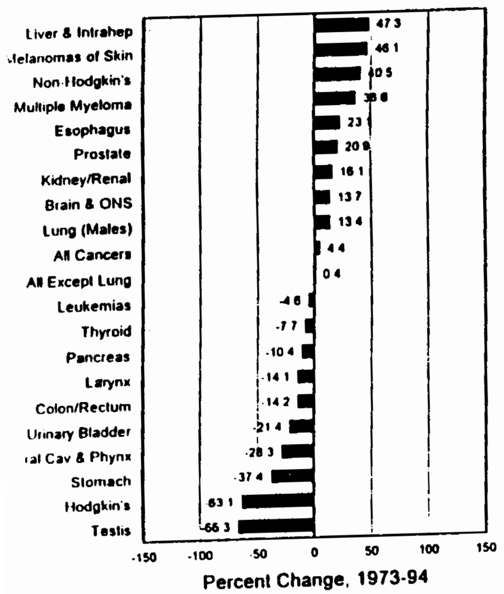


CANCER FACTS & FIGURES 1997

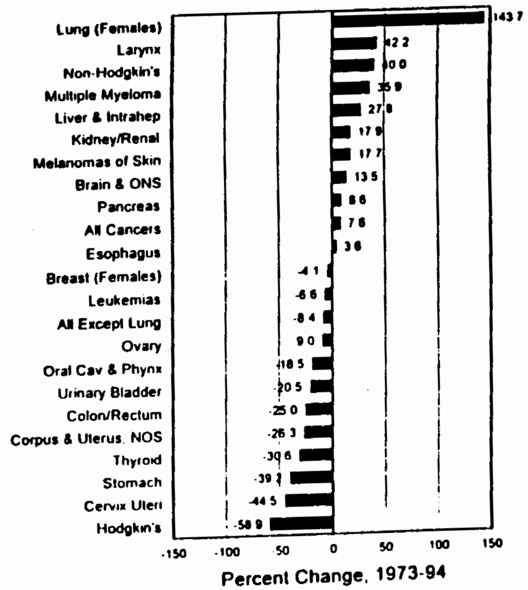
Trends in U.S. Mortality Rates by Primary Cancer Site 1973-1994

(3)

All Races, Males



All Races, Females



TRENDS IN SEER INCIDENCE§ AND U.S. MORTALITY& FOR SELECTED CANCER SITES, 1973-94

All Races, Males and Females⊕

Mortality PC Incidence PC

Decreasing Mortality / Decreasing Incidence

Site	Mrt	Inc
Oral cavity & Pharynx	-24.7	-6.5
Stomach	-37.9	-20.0
Colon & Rectum	-19.6	-5.2
Pancreas	-1.6	-10.5
Larynx	-6.0	-11.4
Cervix uteri⊕	-44.5	-40.6
Corpus & Uterus, NOS⊕	-26.3	-27.9
Hodgkin's disease	-61.5	-15.5
Leukemias	-5.7	-9.3

Decreasing Mortality / Increasing Incidence

Site	Mrt	Inc
Breast⊕	-4.1	23.0
Ovary⊕	-9.0	0.5
Testis⊕	-66.3	50.6
Urinary Bladder	-22.4	11.6
Thyroid	-22.9	31.6

Increasing Mortality / Decreasing Incidence

(none)

Increasing Mortality / Increasing Incidence

Site	Mrt	Inc
All sites	5.4	23.4
Esophagus	10.6	11.2
Liver & Intrahep	39.5	61.0
Lung & Bronchus	40.0	31.4
Melanomas of skin	33.2	113.0
Prostate⊕	20.9	141.0
Kidney & Renal pelvis	16.3	42.9
Brain & Other nervous	13.5	10.5
Non-Hodgkin's lymphomas	39.9	80.6
Multiple myeloma	35.0	14.4

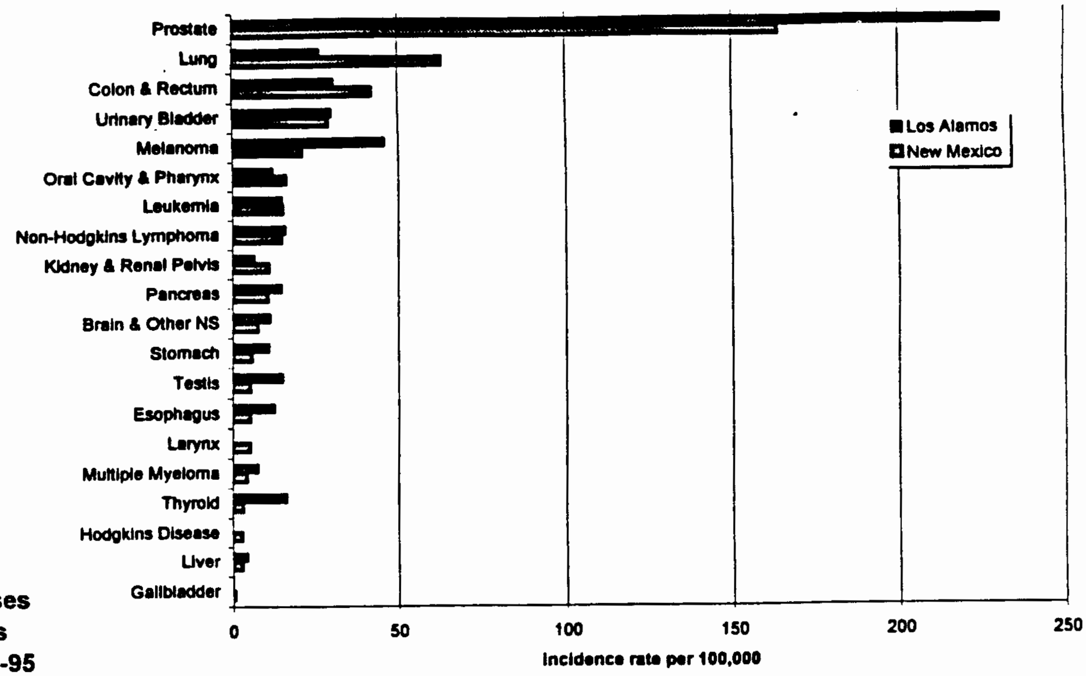
Note: PC is the Percent Change over the time interval.

⊕ PCs for sex specific sites are only for the proper sex. PCs for breast cancer are for females only.

§ SEER Program. Rates are per 100,000 and are age-adjusted to the 1970 U.S. standard population.

& NCHS public use tape. Rates are per 100,000 and are age-adjusted to the 1970 U.S. standard population.

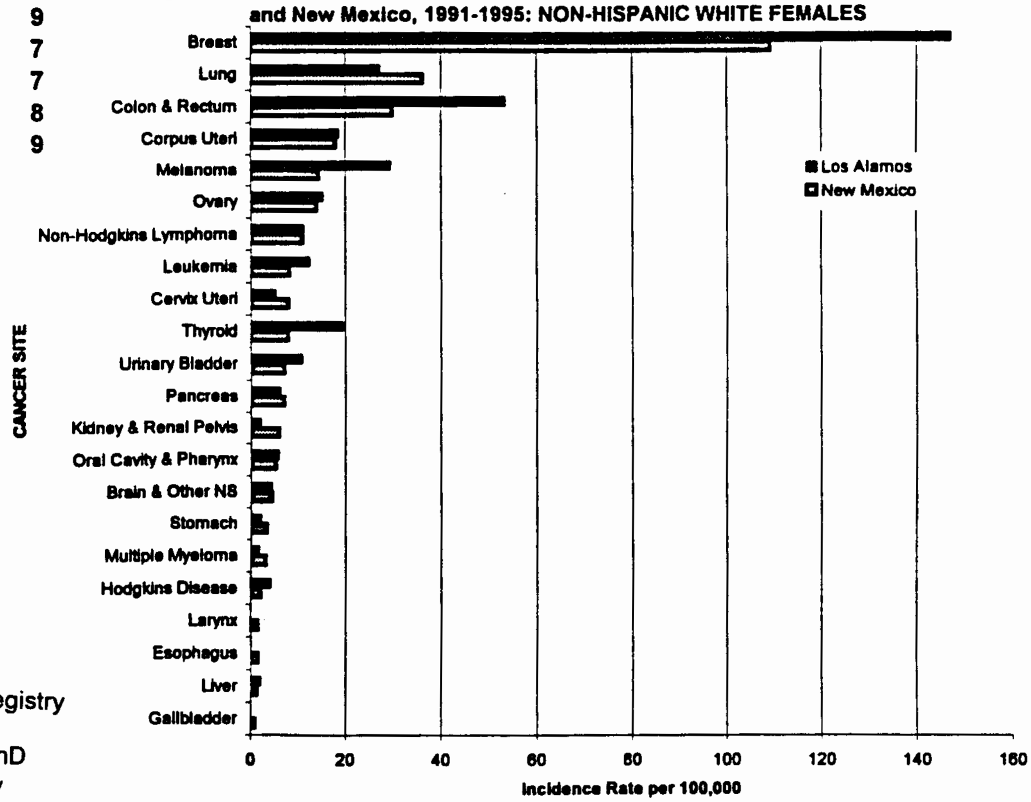
Average annual age-adjusted incidence rates for selected cancer sites: Los Alamos and New Mexico, 1991-1995 NON-HISPANIC WHITE MALES



number of cases
5-year totals

	1986-90	1991-95
Breast	68	83
Prostate	48	100
Colon & Rectum	28	44
Melanoma	27	30
Lung	34	22
Thyroid	17	18
Lymphoma	13	12
Leukemia	10	13
Corpus Uteri	10	9
Ovary	11	7
Brain	8	7
Urinary Bladder	5	8
Pancreas	4	9

Average annual age-adjusted incidence rates for selected cancer sites: Los Alamos county and New Mexico, 1991-1995: NON-HISPANIC WHITE FEMALES

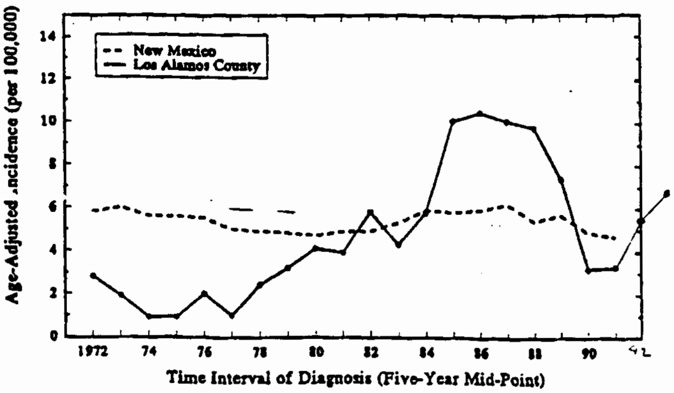


Source:

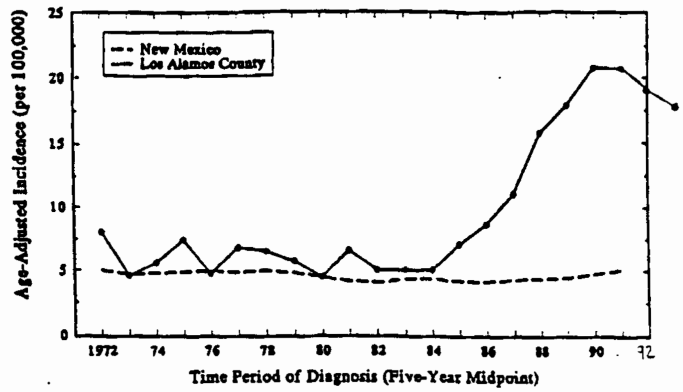
New Mexico Tumor Registry

Charles R. Key, MD PhD
Professor of Pathology
Medical Director, New Mexico Tumor Registry
UNM Cancer Research and Treatment Center

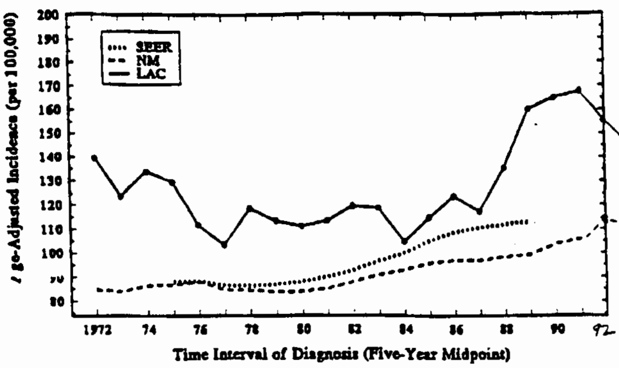
Five-Year Average Annual Incidence of Brain & Nervous System Cancer: Los Alamos County and New Mexico, Both Sexes, All Races, 1970-1995



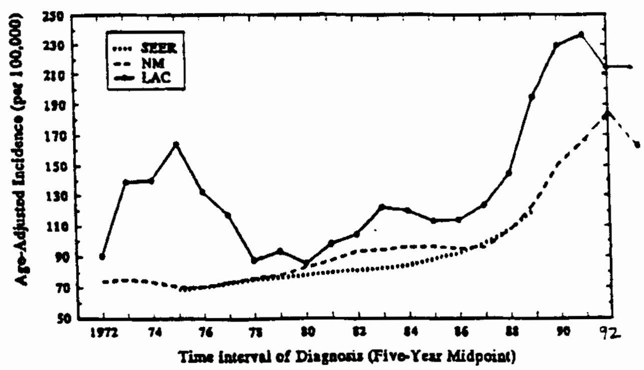
Five-year Average Annual Incidence of Thyroid Cancer: Los Alamos County and New Mexico, Both Sexes, All Races, 1970-1995



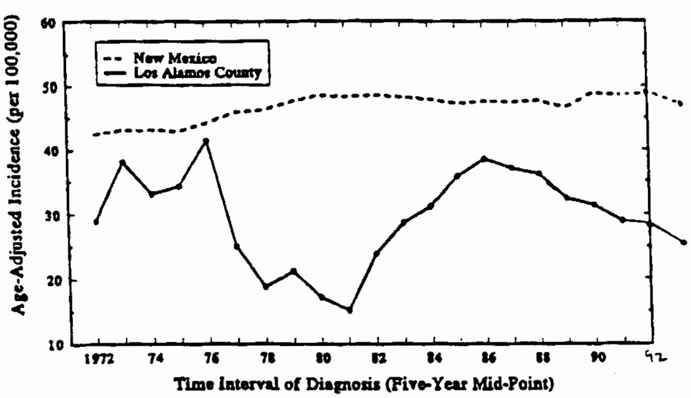
Five-Year Average Annual Incidence of Female Breast Cancer: LAC and NM Non-Hispanic Whites, SEER Whites, 1970-1995



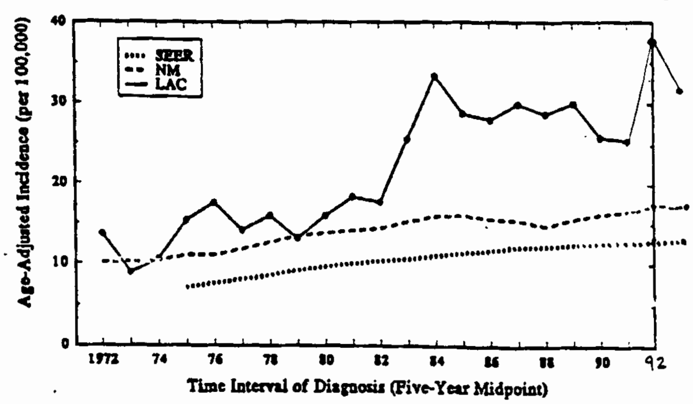
Five-Year Average Annual Incidence of Prostate Cancer: LAC and NM Non-Hispanic Whites, SEER Whites, 1970-1995



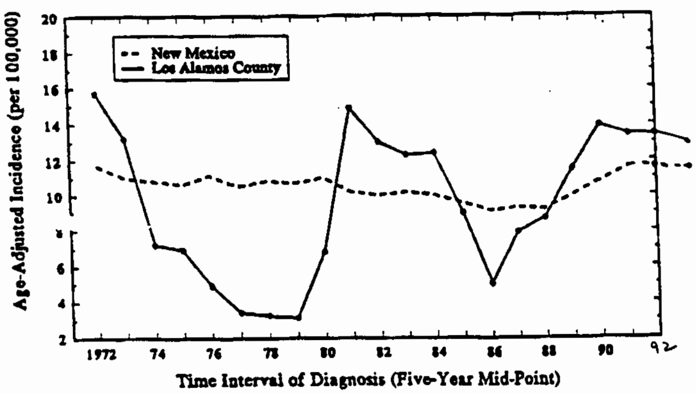
Five-Year Average Annual Incidence of Lung Cancer: Los Alamos County and New Mexico, Non-Hispanic Whites, Both Sexes, 1970-1995



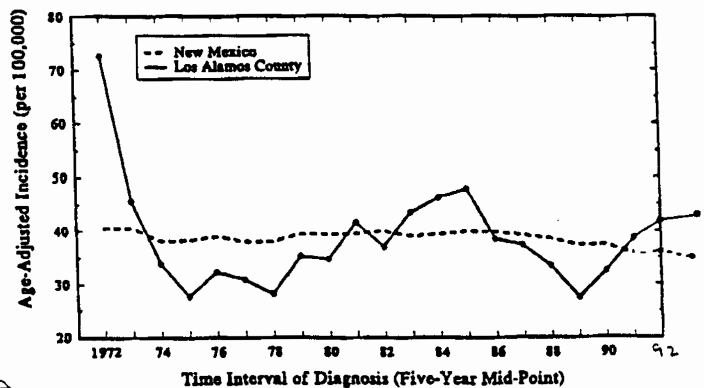
Five-Year Average Annual Incidence of Melanoma of Skin: LAC and NM Non-Hispanic Whites, SEER Whites, Both Sexes, 1970-1995



Five-Year Average Annual Incidence of Leukemia: Los Alamos County and New Mexico, Non-Hispanic Whites, Both Sexes, 1970-1995



Five-Year Average Annual Incidence of Colo-Rectal Cancer: Los Alamos County and New Mexico, Non-Hispanic Whites, Both Sexes, 1970-1995



INVESTIGATION OF EXCESS THYROID CANCER INCIDENCE IN LOS ALAMOS COUNTY

GREAT SEAL OF THE STATE OF NEW MEXICO · 1912 ·
Crescit Eundo

William F. Athas Ph.D.
New Mexico Department of Health
Division of Epidemiology, Evaluation, and Planning
Santa Fe, New Mexico 87502
April, 1996

This study was supported by funds from the Office of Epidemiology and Health Surveillance, U.S. Department of Energy, Grant No. DE-FG04-91AL75237

ACKNOWLEDGMENTS

The author would like to extend thanks to the members of the Thyroid Cancer Technical Steering Sub-Committee for their helpful comments and criticisms (Scott Davis Ph.D., Earl Ford M.D., Frank Gilliland M.D., Don Morris M.D., Gerry Petersen Ph.D., and Helen Stanbro M.S.); to Michael Jackson M.D. at the Los Alamos Medical Center for valuable discussions regarding thyroid surgery; to George Voelz M.D. and Laurie Wiggs Ph.D. at the Los Alamos National Laboratory for discussion and assistance; and to Charles Key M.D. at the New Mexico Tumor Registry for technical assistance and overall support.

Special thanks to Jon Johnson M.D. for conducting the preliminary thyroid cancer case review; and to Sharon Bennett, Marge Luther, and the rest of the staff at the Los Alamos Medical Center Health Information Department for assistance with the medical records review.

EXECUTIVE SUMMARY

Los Alamos County (LAC) is home to the Los Alamos National Laboratory, a U.S. Department of Energy (DOE) nuclear research and design facility. In 1991, the DOE funded the New Mexico Department of Health to conduct a review of cancer incidence rates in LAC in response to citizen concerns over what was perceived as a large excess of brain tumors and a possible relationship to radiological contaminants from the Laboratory. The study found no unusual or alarming pattern in the incidence of brain cancer, however, a fourfold excess of thyroid cancer was observed during the late-1980's. A rapid review of the medical records for cases diagnosed between 1986 and 1990 failed to demonstrate that the thyroid cancer excess had resulted from enhanced detection. Surveillance activities subsequently undertaken to monitor the trend revealed that the excess persisted into 1993. A feasibility assessment of further studies was made, and ultimately, an investigation was conducted to document the epidemiologic characteristics of the excess in detail and to explore possible causes through a case-series records review. Findings from the investigation are the subject of this report.

The scope of the investigation was limited to an examination of descriptive epidemiologic data and individual data abstracted from patient medical records and Laboratory health physics records for all cases of thyroid cancer newly diagnosed among LAC residents between 1970 and 1995. Cases were identified through review of the casefile of the New Mexico Tumor Registry, a statewide population-based cancer registry located at the University of New Mexico Cancer Center. The data analysis presented was guided by two principal questions. The first was the extent to which temporal changes in the detection or diagnosis of thyroid cancer among LAC residents could have accounted for the recent excess. The second was the extent to which established or suspect thyroid cancer risk factors could have accounted for the excess. Although the role of environmental hazards could not be directly assessed due to an absence of exposure data, information was collected on county residence characteristics in order to examine issues of latency and migration.

Results of the investigation showed the incidence of thyroid cancer in LAC fluctuated slightly above the statewide incidence between 1970 and the mid-1980's before rising to a statistically-significant fourfold elevated level during the late-1980's and early-1990's. Age-adjusted thyroid cancer incidence in LAC during 1988-1992 was 20.7 per 100,000 (n=22, 95% CI= 12.6- 30.9) compared to 4.5 per 100,000 in the state. The high rate was sustained briefly, then began to decline as decreasing numbers of cases were diagnosed during 1994 and 1995. If statewide incidence rates had prevailed in the county between 1988 and 1995, one would have expected about eight cases (two to three males and five to six females). Instead, 31 cases (12 males, 19 females) were observed. Thus, the recent elevation in incidence was based on roughly 23 excess cases. Examination of the incidence of thyroid cancer in surrounding counties (Santa Fe, Rio Arriba, Taos, Sandoval) showed that the excess was geographically localized to LAC.

The investigation found little evidence that the higher than expected number of cases could be accounted for by temporal changes in the manner of thyroid cancer detection or diagnosis among LAC residents. The majority of all cases were detected following palpation of an asymptomatic neck mass by health care practitioners located at the local community hospital or the Laboratory. None of the thyroid cancer cases had been detected by thyroid ultrasonography, nor was a temporal shift towards more incidental diagnoses of small occult thyroid cancers observed. A notably higher percentage of male cases had their tumor discovered at the Laboratory compared to females, suggesting an impact from occupational medical surveillance. Close medical surveillance and greater access to medical treatment were population attributes which likely facilitated the recent excess in LAC.

Review of the descriptive epidemiology of thyroid cancer in LAC yielded a pattern of contrasts between males and females which suggested dissimilar etiologies. LAC males experienced an unprecedented fivefold excess of thyroid cancer during 1988-1995 which was distinguished not only by its magnitude and rapidity of onset, but also by a broad age distribution and a heterogenous mix of cell types, including two rarely diagnosed histologic forms. In contrast, LAC females experienced a smaller threefold excess in incidence which was localized to women between the ages of 30 and 59 years, and which had been preceded by an elevated background incidence similarly localized to women in this age range. The female excess also was distinguished by a near exclusive involvement of one histologic cell type, i.e., papillary carcinoma.

Analysis of the case-series review data provided results similarly suggesting the excess was multi-factorial in etiologic origin with differing risk factors for males and females. Established risk factors identified among the case series included genetic susceptibility (e.g., medullary carcinoma) and prior therapeutic irradiation to the head and neck. Suspect risk factors included occupational radiation exposure, parental history of thyroid surgery for nodular disease, and overweight. The prevalence of genetic susceptibility and prior radiation exposure was notably higher in males than females. Among the female cases, a notable recent shift toward overweight was observed, suggesting a changing underlying prevalence of host risk factors in LAC females.

Based on latency and histopathologic considerations, it is estimated that a putative local community exposure to ionizing radiation could have accounted for no more than 23 of the 31 (74%) thyroid cancer cases diagnosed between 1988 and 1995. Excluding cases which had received therapeutic irradiation to the head and neck, the etiologic portion which could be attributed to a hypothetical community exposure was further reduced to 67% of the cases. A more detailed study of the potential impact from local environmental hazards would require data which defines the geographic, temporal, and dosimetric dimensions of exposure. Results obtained from this investigation showed that the 1988-1995 cases included persons who had moved to LAC at different points in time and had lived in the county for varying lengths of time prior to diagnosis. Most of the cases had not lived in LAC prior to 1970, only about half had resided in the county more than 20 years prior to diagnosis, roughly 20% had resided in the county two years or less prior to diagnosis, and only four had resided in LAC during childhood.

The investigation described in this report did not identify a specific cause of the unusually high number of thyroid cancers recently diagnosed in LAC. The likelihood is that the excess had multiple causes, some of which have been examined in this investigation, and some of which may never be identified. This has been the general experience of investigations of elevated cancer rates in communities around the country. By and large, the policy developed to deal with these issues has been to monitor locations where excesses have occurred, look for further clues among additional cases, and re-evaluate new data if it becomes available. It is this policy which is recommended here. Surveillance data collected for 1994 and 1995 already has suggested that the excess which began in the late-1980's is now declining.

RECOMMENDATIONS

- Continue to monitor the incidence of thyroid cancer in LAC using cancer case data routinely collected by the NMTR.
- Continue to abstract and analyze epidemiologic and clinical information from the medical records of newly diagnosed cases of thyroid cancer in LAC.
- Re-evaluate the case information collected through the records review if indicated by new information on environmental exposures or other risk factors.

TABLE OF CONTENTS

TABLES

FIGURES

INTRODUCTION

Los Alamos County (LAC) is located on the east slope of the Jemez mountains in north-central New Mexico roughly 25 miles to the northwest of Santa Fe. The county is home to the Los Alamos National Laboratory (the Laboratory), a U.S. Department of Energy (DOE) nuclear research and design facility. The Laboratory and the adjacent town of Los Alamos were created by the U.S. government in 1943 to serve as the site of Project Y of the Manhattan Engineer District, the top-secret wartime effort to build the atomic bomb. The county of Los Alamos was created in 1949 from 109 square miles of land apportioned from neighboring Santa Fe and Sandoval counties. The surrounding land was then, as it remains today, sparsely populated and virtually undeveloped. A series of finger-like mesas separated by deep east-to-west oriented canyons dominate the regional geography, and as such, add to the sense of remoteness and inaccessibility of the location.

During the war years Los Alamos was inhabited primarily by military personnel, scientists, technicians, and their families. The military presence diminished following World War II, however, the civilian community continued to grow in support of the expanding nuclear weapons research and design mission of the Laboratory. Growth in the population was fueled largely by the influx of highly-educated non-Hispanic whites emigrating from various parts of the country to work at high-paying scientific and engineering positions at the Laboratory. In 1990, the U.S. Census enumerated 18,115 residents in the county. Two thirds lived in Los Alamos, and the remainder in White Rock, a suburban "bedroom" community located eight miles to the southeast of Los Alamos. The county population was 85% non-Hispanic white, 11% Hispanic, and 4% other races. Twenty-six percent of the population was less than 18 years of age, 65% aged 18 to 64 years, and 9% aged 65 years and older. Thirty percent of the total population had been born in New Mexico, and of those five years of age and older, 70% had lived in the county since 1985.

LAC ranked first among all U.S. counties with respect to the percentage of adults with a bachelor's degree (53.4%) in 1990. Of county residents 25 years and older, 30% held a graduate or professional degree. The median family income in 1989 was $60,798; fourth highest among all U.S. counties. Of those 16 years of age and older, 83% of males and 63% of females were in the labor force, 2% were unemployed, and 49% were employed in managerial and specialty occupations. Among males, the majority were employed as engineers or natural scientists (33%), technicians (18%), and administrators and managers (13%). Among working females, the majority were employed as administrative support personnel (25%), administrators and managers (14%), technicians (11%), and teachers, librarians, or counselors (10%). The county population accesses medical treatment primarily at the Los Alamos Medical Center (LAMC), a 53-bed community hospital built by the U.S. government in 1950.

In the spring of 1991, residents of the county expressed concern over what was alleged to be a recent large excess of brain tumors and a possible relationship to radiological contaminants from the Laboratory. In response, the DOE funded the New Mexico Department of Health (NMDOH) to conduct a comprehensive review of cancer incidence rates in LAC. The study was formally launched in December of 1991 with a public meeting of the Steering Committee (SC), a 13-member panel convened by the NMDOH to provide technical assistance and scientific oversight on the study. The SC consisted of local residents, Laboratory representatives, several local and out-of-state public health professionals, and representatives of various Federal health agencies. As defined at the first SC meeting, the primary goal of the study was to examine total and site-specific cancer incidence among LAC residents from 1970 to 1990 to look for and evaluate unusual or unexpected patterns and trends. Of primary interest to the community was whether an excess of brain cancer had occurred, and if so, it's magnitude, geographical distribution within the county, and likelihood of being related to Laboratory-related radiation exposures.

All cancer incidence rate data for the study were supplied by the New Mexico Tumor Registry (NMTR), a statewide population-based cancer registry located at the University of New Mexico Cancer Center. The NMTR has been in operation since 1967, and has been a participant in the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) Program since 1973. The methodologic approach to the study was to calculate five-year average annual age-adjusted cancer incidence rates for LAC and to compare the county rates to corresponding State of New Mexico and U.S. SEER rates based on a five-year moving average approach. Thus, beginning with the five-year time period 1970-1974, and proceeding by one year increments up through the final five-year time period 1986-1990, a total of 17 incidence rates and incidence rate ratios were examined in tabular format for each cancer site. In all, cancer incidence rates and incidence rate ratios for 22 major sites and childhood cancers were reviewed and the results presented in a report issued in March of 1993 (2).

The study found an overall pattern of cancer incidence in LAC which generally conformed to what one might expect for an affluent, highly-educated population under close medical surveillance. Among the major cancers, modest excesses of breast and prostate cancer and deficits in lung cancer were observed. No particularly unusual or alarming pattern in the incidence of brain cancer was found. Reconciliation of the study results with citizen claims of a large excess of brain tumors revealed that many of the alleged cases identified by residents as part of the excess involved metastatic brain disease or nervous system tumors diagnosed among former residents of the county. Based on these findings, a recommendation was made that no study further study of brain tumors in LAC was needed beyond routine surveillance of brain cancer.

One study finding which did not fit the overall profile was a large increase in the incidence of thyroid cancer during the late-1980's. Thyroid cancer incidence in LAC was relatively stable and marginally elevated by 10% to 15% from 1970 up until the mid-1980's, at which time an increase began to occur. By the final five-year time period 1986-1990, thyroid cancer incidence in LAC had risen to a statistically-significant near fourfold level over that in the state. The age-adjusted incidence in LAC during 1986-1990 was 15.8 per 100,000 (n=17, 95% CI= 8.5-25.4) compared to 4.4 per 100,000 for the state. Six of the 17 cases occurred in males and all cases were older than 18 years of age at diagnosis.

The sudden and marked rise in incidence was at first glance thought to be indicative of the introduction of a new or improved detection modality. Advances in ultrasonography allowing for detailed visualization of the thyroid had been achieved during the mid-1980's, and thus it was hypothesized that the recent excess in LAC had resulted from the diagnosis of thyroid cancers discovered by intentional or incidental ultrasonic imaging of the thyroid or neck region. A rapid review of the medical records for cases diagnosed between 1986 and 1990, however, failed to provide evidence that any case had been detected by ultrasonography. The prospect that the excess was an artifact of screening was further dampened by a review of data routinely compiled by the NMTR on tumor size at diagnosis. These data showed that on average the thyroid cancers diagnosed among LAC residents between 1986 and 1990 were no smaller, and perhaps even slightly larger, than those diagnosed across the remainder of the state during the same time period. Based on these findings, recommendations were included in the report to monitor the incidence of thyroid cancer in LAC and to assess the feasibility of a case-control study to identify possible causes of the excess.

As a prelude to planning future study activities a comprehensive review of the scientific literature on thyroid cancer was conducted in the spring of 1993. The literature review revealed that thyroid cancer is a rare malignancy which accounts for an estimated one percent of all cancers diagnosed annually in the U.S. (36) The disease occurs two to three times more frequently in women than in men, and is particularly common among young and middle-aged women. The majority of thyroid cancers are slow-growing, indolent tumors which rarely are fatal. The disease is highly treatable and mortality is about ten times lower than incidence. Four major histologic types occur. Each displays a different epidemiologic pattern and represents a different biologic entity. The most common histologic type is papillary carcinoma (75%) followed by follicular (18%), medullary (3%), and anaplastic (3%). All arise from follicular epithelial cells except the medullary form, which originates from the parafollicular C-cells of the thyroid.

Thyroid cancer typically presents as a focal asymptomatic thyroid mass (i.e., nodule) detected either by the patient or their health care practitioner during a physical exam. Since thyroid nodules are highly prevalent (4%-7%) in the general adult population, and most are benign, patients are selected for surgery based on the likelihood of malignancy being present (25). Age, sex, medical history, nodule characteristics, patient preference, and surgeon philosophy are all factors which influence the decision to either follow the lesion or proceed with surgery (26). Fine-needle aspiration biopsy (FNAB) of thyroid nodules increasingly has been used over the past decade in the U.S. to establish a preoperative diagnosis (13). Occasionally, incidental diagnoses of thyroid cancer are made based on the presence of small (<5 mm) occult foci of papillary carcinoma found at surgery for nodules which ultimately prove to be benign. Although the incidence of clinical papillary carcinoma is relatively low, occult papillary carcinomas are believed to be present in a substantial portion of the general population. Estimates based on careful histopathologic examination of thyroid tissue at autopsy show the prevalence rate of occult thyroid carcinoma to vary between 6% and 36% (18,24).

The etiology of thyroid cancer is not well understood and likely varies by gender and histologic type (9). Ionizing radiation is a known cause of papillary carcinoma, and possibly follicular and anaplastic carcinoma (40). Dose-dependent excess risk has been demonstrated in a number of irradiated populations including persons treated in childhood with X-ray therapy for benign head and neck conditions (39), the Japanese A-bomb survivors (30), and persons exposed to fall out radiation from Pacific Islands atmospheric nuclear weapons testing (17). Persons exposed during early childhood are more prone to develop thyroid cancer than those exposed as adolescents and adults. Evidence also exists that persons occupationally exposed to external ionizing radiation, such as X-ray technicians, may be at increased risk of thyroid cancer (3,43,45). The level of excess risk, if any, associated with low level environmental exposures to ionizing radiation is unknown. Studies of populations living in areas of high natural background radiation (42,32) and in proximity to nuclear installations (4,35) have not shown evidence for an increased risk. Diagnostic x-rays, the largest manmade source of exposure to ionizing radiation for the general population, are not believed to measurably increase the risk of thyroid cancer (19).

Apart from ionizing radiation, little else is conclusively known about thyroid cancer causation. Genetic factors play a role in medullary carcinoma, which often presents as a familial disease (10). A familial form of papillary carcinoma also may exist (16). The striking female predominance during the childbearing years has lead to a number of studies of reproductive and hormonal factors (1,11,23,28,38), however, consistent results have not been observed. It has been hypothesized that elevated levels of endogenous or exogenous female sex hormones lead to elevated levels of thyroid stimulating hormone (TSH), which in turn promotes hyperplasia of the thyroid, and thus increases the risk of thyroid cancer. It has also been suggested that female thyroid cancer and breast cancer share similar etiologic factors since these two cancers occur as multiple primaries more often than would be expected by chance alone (29,37). Personal history of breast cancer, overweight, and prior radiation exposure have been identified as risk factors likely common to both thyroid and breast cancer (29). Overweight has been observed to increase the risk of thyroid cancer among both males (15) and females (15,20,29,34,38).

Antecedent benign nodular thyroid disease consistently has been found to increase thyroid cancer risk (22,27,33,34,38). The extent to which these lesions are involved in the natural history of thyroid cancer or simply induce closer medical surveillance for thyroid cancer is unknown. Family history of benign thyroid disease, particularly in the form of nodular disease (5,20,22, 31,34,44), also has been associated with the subsequent development of thyroid cancer. Although information about diet and thyroid cancer is relatively crude, a protective effect from cruciferous vegetables has been observed (20), whereas some seafoods have been linked to an increased risk (20). The role of dietary iodine (7,12,14), and chemical or dietary goitrogens (5,8) in the development of thyroid cancer remains unclear.

In the summer of 1993, the NMDOH convened a seven-member Thyroid Cancer Technical Sub-Committee (TSC) of the SC to assess the feasibility of a case-control study of thyroid cancer in LAC. The case-control approach begins with a defined population of persons with and without the disease of interest and compares the prevalence of potentially causative risk factors in both groups. Complicating the matter is the fact that critical exposures for many forms of cancer, including thyroid cancer, typically occur decades prior to diagnosis. For example, the average latency of radiation-induced thyroid cancer in adults has been estimated to be on the order of two to four decades. Thus, one major issue of concern when considering a case-control study of cancer is the extent to which data can be accurately collected on distantly past exposures thought to be relevant to the development of the cancer under study.

The TSC first met in November of 1993 to examine issues relating to potential test hypotheses, sample size considerations, potential control populations, and overall methodologic limitations. Of primary concern to the TSC was the absence of a specific hypothesis linking the thyroid cancer excess to a particular exposure or risk factor in LAC. Although the issue of Laboratory-related community radiation exposures had been discussed at length at various public forums as a result of the alleged brain tumor cluster, no specific exposure information had emerged from the discussions which could be used to formulate a hypothesis relating to the thyroid cancer excess. Moreover, the task of identifying and quantifying potentially important past community radiation or chemical exposures (i.e., dose-reconstruction) was significant. Spokespersons for the Centers for Disease Control (CDC) Radiation Studies Branch indicated at several public meetings in LAC during 1992 and 1993 that a full-scale study would require an expertise in dose-reconstruction, take years to complete, and cost several million dollars. Given these circumstances, the TSC felt it premature to consider an analytic case-control study of thyroid cancer and environmental exposures in LAC.

The absence of a specific exposure hypothesis did not necessarily preclude a case-control study. One alternative discussed by the TSC was to conduct an "exploratory" analysis as a "hypothesis-generating" exercise. Such a study would again require significant resources, yet harbor a potential only for advancing a hypothesis for a more detailed investigation. Another study design considered to be a more efficient first look is the case-series review, essentially a case-control study without the controls. The case-series review approach is particularly justified in situations involving rare diseases with large observed risk ratios. Under such conditions, most of the cases will be "excess" cases, and thus, any singular explanatory variable would have to be one which is shared by a majority of cases. The recent thyroid cancer excess in LAC clearly met these conditions. Between 1988 and 1993, 27 cases of thyroid cancer had been diagnosed in the county, of which only about seven would have been expected. Thus, an excess of roughly 20 cases had occurred. Given these circumstances, the NMDOH chose to implement a case-series review as the principal public health response to the observed thyroid cancer excess in LAC.

Purpose and Scope of the Investigation

The purpose of the investigation was to document in detail the epidemiologic characteristics of the recent thyroid cancer excess in LAC and to explore possible causes through a case-series records review. The scope of the investigation was limited to an analysis of descriptive epidemiologic data and individual case data abstracted from patient medical records and Laboratory health physics records for all cases of thyroid cancer newly diagnosed in LAC residents between 1970 and 1995. Two basic questions guided the investigation. The first was the extent to which the recent excess, as defined temporally by the time period 1988-1995, could have been caused by changes in the detection or diagnosis of thyroid cancer among LAC residents. Of particular interest was a possible change in the prevalence of practitioner-detected thyroid cancers. The second question sought to ascertain the extent to which established or suspect risk factors could have accounted for the recent excess. Of particular interest here was the extent to which the cancer excess displayed a common etiologic profile, or alternatively, appeared to be of multi-factorial etiologic origin.

METHODS

Case Definition and Ascertainment

The cancer cases evaluated in this report were defined as residents of LAC who were newly diagnosed with a primary thyroid cancer between January 1, 1970 and December 31, 1995. All cases were identified through review of the NMTR cancer casefile. A total of 54 incident cases of thyroid cancer were included in the analysis, including one case diagnosed at autopsy in 1976. Rapid casefinding procedures were implemented for 1995, and it is possible, although unlikely, that additional 1995 cases may be found.

Descriptive Epidemiology

Thyroid cancer incidence rates were calculated using case numerators and U.S. census-derived population denominators supplied by the NMTR. Except for age-specific rates, all incidence rates were age-adjusted in five-year categories to the 1970 U.S. population by the direct method. For descriptive analysis, age-, sex- and, histologic-specific incidence rates were calculated for LAC and compared to corresponding State of New Mexico referent rates. Ninety-five percent confidence intervals (95% CI) for the LAC rates were generated using the Poisson-based method of Dobson et. al. (6). Statistical elevation in LAC incidence was defined as exclusion of the state referent rate by the lower confidence limit of the subject LAC rate, or mutual exclusion of confidence limits for county rates.

Case-Series Records Review

A review of case medical records was conducted between April 1994 and January 1996 by the author using a pre-coded standard data abstraction form. The autopsy case was excluded from analysis. Of the remaining 53 cases, 47 had been diagnosed at the LAMC and the remaining six at hospitals in Santa Fe and Albuquerque. Medical charts at the location of thyroid surgery were reviewed for all cases. All cases were found to have a LAMC medical chart and each was reviewed regardless of location of surgery. Data were abstracted from the patient medical charts on a range of variables relating to the detection, clinical evaluation, and diagnosis of thyroid cancer; patient medical history; radiation exposure history; and height and weight at thyroid surgery. Information obtained on demographic variables included typical occupation, date of entry into LAC, and first LAMC medical chart entry. Copies of surgical pathology reports were obtained for all cases and extent of disease at diagnosis coded according to the classification scheme in TNM Atlas 3rd Edition, 2nd Revision, UICC (Springer-Verlag, Berlin, 1992).

Laboratory health physics records were reviewed to identify all cases of non-medullary thyroid cancer among persons greater than 20 years of age at diagnosis who had ever been monitored for radiation exposure at the Laboratory. The analysis was limited in time to eligible cases diagnosed between 1970 and 1993. The main variable of interest was cumulative dose of whole-body external penetrating radiation. All data were abstracted by a single Laboratory staff person familiar with the health physics records but unaware of the specific purpose of the study and blinded to the health status of the study subjects. The variable of interest was calculated by taking the sum of the cumulative annual measurements of gamma and neutron forms of radiation (rem) received up to two years prior to diagnosis.

Analysis procedures for the case-series review data involved routine univariate distribution statistics. All analyses were gender-specific. Because of the small sample size, temporal analyses were conducted using two aggregate time periods: 1970-1987 and 1988-1995. The later time period was taken as the defined time interval of excess thyroid cancer incidence in LAC

Confidentiality

Case confidentiality was assured throughout all phases of the investigation by routine security procedures. A unique study number was assigned to each case; all study forms and databases lacked personal identifiers; personal identifiers were immediately removed from copies of pathology reports and replaced by case study numbers; and the code list matching personal identifiers and study numbers was kept in a secured location. Only the author had access to the match list, and the author was the only study member who accessed case medical records. All medical records were abstracted within the health information systems unit within each respective hospital.

RESULTS

Descriptive Epidemiology

Fifty-four cases of thyroid cancer were newly diagnosed among LAC residents (17 males, 37 females) over the 26-year time period 1970-1995. The distribution of cases by year of diagnosis and sex is shown in Figure 1. More than half of the cases were diagnosed between 1988 and 1995, including 51% of the female cases and 71% of the male cases. Table 1 gives the distribution of cases by age at diagnosis and sex. Age at diagnosis ranged from six to 77 years. The age distribution for female cases was tightly clustered between the ages of 30 and 59 years. Among males, age at diagnosis was more broadly distributed and showed a trend of increasing diagnoses with advancing age. The median age at diagnosis was ten years younger for females (39 years) compared to males (49 years). The majority of the cases were non-Hispanic white, including 16 of 17 (94%) males and 33 of 37 (89%) females. The remaining five cases involved persons of Hispanic origin. One case is known to have died of thyroid cancer.

Table 1
Distribution of Age at Diagnosis by Sex
for Los Alamos County
Thyroid Cancer Case Series, 1970-1995

	Number (percent)	
Age at diagnosis	Males	Females
0-14	1 (6)	2 (5)
15-29	2 (12)	2 (5)
30-44	3 (17)	18 (49)
45-59	7 (41)	13 (36)
60-74	4 (24)	0 (0)
75+	0 (0)	2 (5)
Total	17 (100)	37 (100)

Figure 2 shows the temporal pattern of thyroid cancer incidence in LAC between 1970 and 1995 by five-year moving average time periods. The county incidence fluctuated slightly above the state incidence between 1970 and the mid-1980's before rising to a statistically-significant fourfold excess during the late-1980's and early 1990's. The thyroid cancer incidence rate in LAC during 1988-1992 was 20.7 per 100,000 (n=22, 95% CI= 12.6, 30.9) compared to a state rate of 4.5 per 100,000. The high rate was sustained briefly, then began to decline as decreasing numbers of cases were diagnosed during 1994 and 1995.

Figure 3 displays the temporal pattern of thyroid cancer incidence in LAC and four neighboring county populations between 1970 and 1992. The graph demonstrates that the recent increase in incidence observed in LAC did not occur among surrounding populations. The incidence of thyroid cancer in each of the counties of Santa Fe, Rio Arriba, Taos, and Sandoval, remained roughly stationary and at a level approximating that across the state over the entire time period. Figure 4 displays a scatter plot of incidence rates for all New Mexico counties between 1970 and 1992. The plot demonstrates that the statistically-elevated fourfold excess of thyroid cancer observed in LAC was an unprecedented occurrence among New Mexico county populations. Incidence at the county level typically ranged from zero to 10 per 100,000. Only two counties displayed an incidence which exceeded 15 per 100,000, and both were based on just two cases.

Figure 5 displays the temporal pattern of thyroid cancer incidence in LAC by sex. The graphs show that the recent excess involved concomitant increases in incidence among both males and females, and that both sexes experienced a declining incidence in the last several years. Temporal patterns of incidence preceding the excess were different for males and females, however. Incidence in LAC males closely approximated that seen in the state up until the late-1980's at which time an abrupt increase leading to a sevenfold peak excess occurred. In contrast, incidence among LAC females consistently exceeded that seen in women statewide prior to increasing to a threefold peak excess around 1990. These general patterns are summarized in Table 2 which gives aggregate incidence rate data by sex for the time periods 1970-1987 and 1988-1995. The data show that both LAC males and females experienced an incidence of thyroid cancer during 1988-1995 which was statistically-elevated over that in the state, and nearly so in comparison to the 1970-1987 LAC rates.

Table 2
Average Annual Age-Adjusted Thyroid Cancer Incidence Rates per 100,000
for Los Alamos County (LAC) and New Mexico (NM), 1970-1995
By Sex and Time Period

	Males			Females		
	LAC			LAC		
Time Period	Rate (cases)	95% CI	NM Rate	Rate (cases)	95% CI	NM Rate
1970-1987	2.9 (5)	(0.3 - 8.2)	2.7	9.8 (18)	(5.8 - 15.5)	6.5
1988-1995	13.7 (12)	(7.4 - 23.5)	2.9	19.8 (19)	(11.4 - 30.5)	7.2

Age-specific incidence rate curves for LAC males and females are shown respectively in Figures 6 and 7 for the aggregate time periods 1970-1987 and 1988-1995. Also shown are age-specific incidence rate curves for New Mexico males and females for the 23-year time period 1970-1992. Among males, a pattern of steadily increasing incidence with advancing age was seen with each of the curves. The LAC incidence curve for 1970-1987 closely approximated that for the state, but was clearly elevated several-fold for nearly all age groups during 1988-1995. A temporal pattern of increasing incidence was observed among all male age groups in LAC except the 0-14 age group.

The age-specific curves for females (Figure 7) displayed a different pattern of incidence than that observed for males. Rather than increasing progressively with age, the age-specific incidence in females rose through the third to fifth decades then subsequently plateaued among older New Mexico women while declining in older LAC women. A comparison of the county to the state reveals that a several-fold excess incidence of thyroid cancer historically has existed among LAC women aged 30 to 59 years. The excess incidence became particularly pronounced for women aged 30-44 years during the recent time period 1988-1995. Temporal analysis of the county rates showed a similar pattern to that seen in LAC males, i.e., increasing incidence for all age groups except those aged 0-14 years.

In regards to childhood thyroid cancer, 14 cases were diagnosed in New Mexico children aged 0-14 years during 1970-1987, of which three (21%) occurred in LAC children (two female, one male). The average annual incidence rate of childhood thyroid cancer in LAC during this time period was 3.7 per 100,000 compared to a corresponding state rate of 0.2 per 100,000. All three of the LAC cases were papillary carcinomas. Examination of the statewide geographic distribution of the 14 childhood cases showed that 10 of the fourteen cases were diagnosed in Bernallilo county (n=6) or counties south of Bernallilo county (n=4). One case was diagnosed in Taos county, and the remaining three in LAC. No cases of childhood thyroid cancer were diagnosed in New Mexico between 1988 and 1993.

Table 3 gives the distribution of the LAC thyroid cancer case series by histologic type and sex. The diagnosis of thyroid cancer was histologically confirmed in 53 of 54 cases. The single outstanding case involved a clinically-diagnosed familial medullary carcinoma. Of the remaining 53 cases, the histologic diagnosis was based on surgical specimens in 52 cases and on autopsy material in one case. Thyroid cancer was not the cause of death for the autopsy case. Papillary carcinoma was the most common form of thyroid cancer diagnosed among LAC residents.

Among females, all but three of the 37 cases were papillary cancers. The three remaining cases were follicular carcinomas. In contrast, all four of the major histologic types of thyroid cancer were diagnosed in LAC males. The medullary and anaplastic forms occurred in five of the 17 (30%) male cases. The single male follicular carcinoma was diagnosed at autopsy.

Table 3
Distribution of Histologic Types by Sex for Los Alamos County Thyroid Cancer Case Series, 1970-1995

	Number of cases (percent)	
Histologic Type	Male	Female
Papillary	11 (64)	34 (91)
Follicular	1 (6)	3 (9)
Medullary	3 (18)	0 (0)
Anaplastic	2 (12)	0 (0)
Total	17 (100)	37 (100)

Table 4 gives histologic-specific thyroid cancer incidence rates by sex for LAC and New Mexico during 1988-1995. Among females, only the incidence of papillary carcinoma was statistically-elevated above that in the state. The papillary form accounted for 87% of the total thyroid cancer incidence in LAC females during 1988-1995. A different histologic pattern of incidence was observed for LAC males in that statistically-elevated rates of three major forms were observed. Papillary carcinoma accounted for roughly 70% of the total male incidence while the remaining 30% was due to unusually high rates of medullary and anaplastic carcinoma.

Table 4
Average Annual Age-Adjusted Thyroid Cancer Incidence Rates per 100,000 for Los Alamos County (LAC), 1988-1995 and New Mexico (NM), 1988-1992 By Histologic Type and Sex

	Males			Females		
	LAC			LAC		
Histologic Type	Rate (cases)	95% CI	NM Rate	Rate (cases)	95% CI	NM Rate
Papillary	9.8 (8)	(3.8-18.6)	2.0	17.2 (17)	(9.5-26.8)	5.9
Follicular	0.0 (0)	-	0.1	2.6 (2)	(0.4-8.9)	0.6
Anaplastic	1.9 (2)	(0.3-6.3)	0.1	0.0 (0)	-	0.1
Medullary	2.0 (2)	(0.3-6.6)	0.1	0.0 (0)	-	0.2
All Types	13.7 (12)	(7.4-23.5)	2.5	19.8 (19)	(11.4-30.5)	6.9

Clinical Characteristics

Information on disease detection, clinical evaluation, diagnosis, and pathology was abstracted from the medical records of all female cases and 16 of the 17 male cases. The single male autopsy case was excluded from the analysis. Thus, a total of 53 "clinical" thyroid cancer cases were included in the analysis of clinical characteristics.

Table 5 gives the distribution of the initial manifestation of disease by sex for the LAC clinical thyroid cancer case series. The data show that a majority of male (81%) and female (95%) cases initially presented with an asymptomatic thyroid nodule, typically without associated lymphadenopathy. Both male cases presenting with symptomatic neck masses (pain and/or respiratory distress) involved anaplastic carcinoma. The male case without a discernible thyroid nodule presented with clinical findings strongly suspicious of medullary carcinoma. Two female cases presenting without a discernible thyroid nodule had enlarged supraclavicular lymph nodes palpated.

Table 5
Distribution of Initial Manifestation of Disease by Sex for Los Alamos County Clinical Thyroid Cancer Case Series, 1970-1995

	Number (percent)	
Initial manifestation of disease	Males	Females
Asymptomatic thyroid nodule(s) only	12 (75)	34 (92)
Asymptomatic nodule w/ enlarged nodes	1 (6)	1 (3)
Symptomatic thyroid mass	2 (13)	0 (0)
Enlarged lymph nodes only	0 (0)	2 (5)
Other clinical symptoms	1 (6)	0 (0)
Total	16 (100)	37 (100)

Fifty of 53 patients (94%) diagnosed with clinical thyroid cancer in LAC between 1970 and 1995 had their cancers detected by palpation of a thyroid mass or enlarged regional lymph node either by themselves or their health care practitioner. The three remaining cases were detected by serum calcitonin measurement, chest X-ray, and nuclear thyroid scan. None of the LAC thyroid cancer cases were detected as a result of intentional or incidental ultrasonic imaging of the thyroid. Table 6 gives information on disease detection by sex and time period of diagnosis. The data show that no major change occurred over time in either sex in regards to the percentage of thyroid cancers detected by patients or health care practitioners. Within either time period, a minority of the male and female cases found their own tumors compared to the roughly 75% to 80% of cancers detected by health care practitioners. Among those cancers detected by

What if you can't afford a routine physical exam?

health care practitioners, nearly all were discovered by palpation of an asymptomatic thyroid nodule during a routine physical exam.

Table 6
Distribution of Disease Detection Characteristics by Sex and Time Period of Diagnosis for Los Alamos County Clinical Thyroid Cancer Case Series, 1970-1995

	Males		Females	
Detection of disease	1970-1987	1988-1995	1970-1987	1988-1995
By patient	1 (20)	3 (25)	4 (22)	3 (16)
By health care practitioner	3 (80)	9 (75)	14 (78)	16 (84)
Los Alamos Medical Center	*1*	*5*	*12*	*14*
Los Alamos National Laboratory	*2*	*4*	*2*	*2*
Total	4 (100)	12 (100)	18 (100)	19 (100)

The data in Table 6 also show that all of the LAC cases who had their cancer detected by a health care practitioner (n=42), were at the time being seen at medical facilities located in the county at either the LAMC (n=32) or the Laboratory (n=10). No major change over time occurred in the percentage of male or female cases detected at these two locations, however, a relatively greater percentage of the male cases were detected at the Laboratory compared to the female cases. Overall, 50% of the practitioner-discovered male cases (6/12) were detected at the Laboratory compared to 13% of the corresponding female cases (4/30). A total of 20 different health care practitioners were responsible for detecting 42 cancers in the LAC clinical case series. A review of the frequency at which individual practitioners at the LAMC or the Laboratory detected thyroid cancer among LAC residents failed to demonstrate any unusual temporal pattern or provide evidence that a particular person was responsible for detecting a disproportionally large number of cancers within either time period.

All patients in the LAC clinical case series received some form of clinical thyroid evaluation at the LAMC following the discovery of signs or symptoms suspicious of thyroid cancer. Forty-seven of the 53 cases (89%) ultimately received their entire clinical evaluation, diagnosis, and surgical treatment at the LAMC. Of these 47 cases, 43 (91%) had their thyroid surgery performed by one of two LAMC general surgeons. The six cases not treated at the LAMC (1970-1987, n=3; 1988-1995, n=3) were diagnosed and surgically-treated at hospitals located in Santa Fe or Albuquerque. Virtually all of the LAC cases had been referred to surgical services by primary care physicians. Medical records for six cases (two 1970-1987, four 1988-1995) indicated that the patient had been seen by an endocrinologist prior to surgery.

Table 7 gives information on the utilization of diagnostic imaging studies and fine-needle aspiration biopsy (FNAB) among the LAC clinical case series by time period of diagnosis. The data show a temporal pattern of decreasing use of nuclear thyroid scan in favor of increasing use of thyroid ultrasound and needle biopsy. Nuclear scan was performed on roughly three-quarters (77%) of the cases diagnosed during the early time period compared to less than half (42%) of the 1988-1995 cases. The majority of patients scanned preoperatively with radioisotopes in both time periods were found to have "cold" nodules. Ultrasonic imaging was performed on roughly one-third (32%) of the 1970-1987 cases compared to nearly all (90%) of the 1988-1995 cases.

The first reported use of thyroid ultrasound appeared in the medical record of a case diagnosed in 1979. The majority of cases in either time period who received a thyroid ultrasound were reported to have one or more partially to completely solid nodules visualized. Fine-needle biopsy of thyroid nodules was undertaken in two (9%) of the 1970-1987 cases and eleven (35%) of the 1988-1995 cases. Neither of the needle biopsies performed on the two 1970-1987 cases were reported as malignant. Results of the needle biopsies performed on the 11 1988-1995 cases were reported as malignant (n=3), suspicious (n=5), or non-diagnostic (n=3). Thus, the percentage of cases diagnosed preoperatively by FNAB was 0% for the 1970-1987 cases and 9% (3/31) for the 1988-1995 cases. All other cases (n=50) were diagnosed following surgical biopsy of the thyroid (n=48) or regional lymph nodes (n=2).

Table 7
Utilization of Diagnostic Imaging and Needle Biopsy by Time Period of Diagnosis for Los Alamos County Clinical Thyroid Cancer Case Series, 1970-1995

	Number of cases (percent)	
Diagnostic procedure	1970-1987 (n=22)	1988-1995 (n=31)
Radioisotope scan	17 (77)	13 (42)
Ultrasound	7 (32)	28 (90)
Fine-needle aspiration biopsy	2 (9)	11 (35)

Pathology reports were reviewed for all 53 clinical thyroid cancers diagnosed in LAC residents between 1970 and 1995. No pathologic evidence of malignancy existed for one case of medullary carcinoma diagnosed clinically. Of the remaining 52 cases, five were diagnosed incidentally following the removal of a thyroid nodule which ultimately proved to be benign.

Four of the incidental diagnoses occurred in 1970-1987 females, of which three were occult papillary carcinomas and one was a small follicular carcinoma. The fifth case was an occult papillary carcinoma diagnosed in a 1988-1995 male. All five cancers were less than five mm in diameter.

Table 8 gives information on the extent of disease at diagnosis by sex and time period for the clinical thyroid cancers which received a pathologic diagnosis (n=52). The data show no obvious trend toward less advanced tumors among either sex in the later time period. Among females diagnosed during 1988-1995, 100% of the cancers were greater than one cm in diameter, 16% had invaded beyond the thyroid capsule, and 22% had spread to regional lymph nodes. Among the 1988-1995 males, 82% of the cancers were greater than one cm in diameter, 9% had invaded beyond the thyroid capsule, and 55% had spread to regional lymph nodes. None of the 53 thyroid cancers diagnosed in LAC between 1970 and 1995 had spread to distant sites at the time of diagnosis.

Table 8
Extent of Disease at Diagnosis by Sex and Time Period of Diagnosis for Los Alamos County Clinical Thyroid Cancer Case Series, 1970-1995

	Males		Females	
TNM Classification	1970-1987 (n=4)	1988-1995 (n=11)	1970-1987 (n=18)	1988-1995 (n=19)
T (Tumor)				
≤ 1 cm (T1)	1 (25)	2 (18)	6 (33)	-
>1 - ≤ 4 cm (T2)	3 (75)	7 (64)	8 (45)	12 (63)
>4 cm (T3)	-	1 (9)	-	4 (21)
Beyond capsule (T4)	-	1 (9)	4 (22)	3 (16)
N (Lymph node metasis)				
None (No)	2 (50)	5 (45)	12 (66)	15 (78)
Ipsilateral (N1a)	1 (25)	1 (10)	3 (17)	2 (11)
Other (N1b)	1 (25)	5 (45)	3 (17)	2 (11)
M (Distant metastasis)				
None (Mo)	4 (100)	11 (100)	18 (100)	19 (100)

Etiologic Factors

Therapeutic ionizing radiation

Four of 53 (8%) patient medical records (3 males, 1 female) indicated a history of therapeutic ionizing radiation treatment to the head and neck for benign conditions. All treatments were given during the 1940's and 1950's. Indications for treatment were different for each patient, and included chronic ear infection, enlarged thymus gland, enlarged tonsils, and benign skin condition. All of the thyroid cancers diagnosed among these cases were papillary carcinomas. The time between reported exposure and thyroid cancer diagnosis ranged from 38 to 42 years among the four cases. Three of the four cases were ten years or younger at the time of treatment while the fourth patient was in their early-20's. The age at diagnosis among the four cases ranged from 41 to 62 years. Two cases were diagnosed during 1970-1987 (one male, one female) and two during 1988-1995 (both males).

Antecedent nodular thyroid disease

One of 53 (2%) patient medical records indicated a history of prior thyroid surgery for benign nodules. The case was a female diagnosed with thyroid cancer during the early time period 1970-1987. The patient had received thyroid surgery for benign nodules prior to residing in LAC.

Hereditary factors

Three cases of medullary carcinoma occurred in the LAC clinical thyroid cancer case series, including one apparently sporadic case diagnosed during 1970-1987 and two familial cases diagnosed during 1988-1995. All three cases occurred in males.

Of the 50 cases of non-medullary thyroid cancer, none had a reported history of thyroid cancer among a first degree relative. One female case diagnosed during 1988-1995 reported a history of thyroid cancer among several paternal aunts. Three of the patient records (one male, two females) indicated that a first-degree relative had received thyroid surgery for benign nodular thyroid disease. All three cases were diagnosed during the later time period 1988-1995. The male case had a history of thyroidectomy in the father. The two female cases both had a history of thyroidectomy in the mother. None of the parents apparently had ever resided in LAC. Goiter among both grandmothers was noted for a single male case diagnosed during 1988-1995.

Three patient medical records indicated an extensive family history of cancer at non-thyroidal sites. All three involved familial gastrointestinal cancers, either involving colon cancer (n=2) or stomach cancer (n=1). Of the two cases with a familial history of colon cancer, one was a male diagnosed in 1988-1995, and the other was a female diagnosed during 1970-1987. The case with a history of familial stomach cancer was a female diagnosed during 1970-1987.

Occupation

Table 9 gives the distribution of typical occupation by sex and time period of diagnosis for the LAC clinical thyroid cancer cases >20 years of age at diagnosis (n=49). The data show a marked gender difference but little if any temporal change in reported occupation among the male or female cases. All male cases were reported to be employed as machinists, engineers, physicists or chemists, whereas no female cases were reported to be employed in these occupations. The majority of female cases within either time period were reported to be homemakers, teachers, librarians, or secretaries. Gender differences also were observed for reported employment at the Laboratory. Among males, 100% and 82% of the cases respectively diagnosed during the early and later time periods were reported to be employed at or retired from the Laboratory. In contrast, 25% and 16% of the female cases respectively diagnosed during the early and later time periods were reported to be employed at the Laboratory.

Table 9
Distribution of Typical Occupation by Sex and Time Period of Diagnosis for Los Alamos County Clinical Thyroid Cancer Cases > 20 Years of Age at Diagnosis, 1970-1995

	Males		Females	
Occupation	1970-1987	1988-1995	1970-1987	1988-1995
Homemaker	-	-	6 (39)	5 (26)
Teacher/librarian	-	-	3 (19)	3 (16)
Secretary/bookkeeper	-	-	1 (6)	3 (16)
Retail sales	-	-	1 (6)	2 (11)
Computer operator/analyst	-	-	2 (12)	2 (11)
Nurse	-	-	2 (12)	1 (5)
Medical technologist	-	-	1 (6)	-
Material technician	-	-	-	1 (5)
X-ray technician	-	-	-	1 (5)
Lawyer	-	-	-	1 (5)
Machinist	1 (33)	1 (9)	-	-
Engineer	-	7 (64)	-	-
Physicist	2 (67)	2 (18)	-	-
Chemist	-	1 (9)	-	-
Total	3 (100)	11 (100)	16 (100)	19 (100)

Three patient medical records (two males, one female) noted significant workplace-related exposures to ionizing radiation. Occupational exposure resulting from atmospheric weapons testing field work was reported for each of the male cases. Employment as an X-ray technician was reported for the female case. All three of the cases were diagnosed with non-medullary thyroid cancer during the later time period 1988-1995. None had a reported history of exposure to therapeutic irradiation of the head and neck.

Table 10 presents data abstracted from Laboratory health physics records on radiation exposure monitoring by sex and time period for the adult LAC non-medullary thyroid cancer cases diagnosed between 1970 and 1993 (n=42). The data show a marked gender difference existed in regards to radiation monitoring history. Eighty percent (8/10) of the male cases had been monitored for radiation exposure compared to 16% (5/32) of the female cases. Of the cases which had been monitored, seven of eight (88%) males and two of five (40%) females had a measurable workplace-related cumulative radiation exposure two years prior to the diagnosis. The magnitude of monitored radiation exposures ranged from 0.1 rem up to roughly 12 rem. Three cases (two males, one female) had a cumulative radiation exposure which exceeded one rem (two males, one female). These cases corresponded to the three 1988-1993 cases whose medical records specifically referenced occupationally-related radiation exposures.

Table 10
Distribution of Cumulative External Penetrating Radiation Exposures Monitored at the Los Alamos National Laboratory by Sex and Time Period of Diagnosis for Los Alamos County Non-Medullary Thyroid Cancer Cases >20 Years of Age at Diagnosis, 1970-1993

	Males		Females	
Exposure level (rem)	1970-1987	1988-1993	1970-1987	1988-1993
Not monitored	-	2 (25)	14 (88)	13 (82)
Monitored < 2 years prior to diagnosis	-	1 (12)	1 (6)	-
0.00	-	-	1 (6)	1 (6)
0.01-0.09	1 (50)	2 (25)	-	-
0.10-0.99	1 (50)	1 (13)	-	1 (6)
1.00-4.99	-	2 (25)	-	-
5.00+	-	-	-	1 (6)
Total	2 (100)	8 (100)	16 (100)	16 (100)

Antecedent female breast cancer

Three female cases had been diagnosed with breast cancer either prior to (n=2) or concurrent with (n=1) their diagnosis of thyroid cancer. All involved papillary carcinomas and all occurred among women diagnosed with thyroid cancer during the later time period 1988-1995.

Thus, 16% (3/19) of the 1988-1995 female cases had a history of breast cancer compared to none of the 1970-1987 female cases. Two of the three cases occurred in women less than 40 years of age at breast cancer diagnosis. A history of breast cancer in either the mother or grandmother was reported for each of these cases, and each had their thyroid cancer detected during a routine follow-up exam for breast cancer. All three cases had their thyroid cancer detected by health care practitioners following palpation of an asymptomatic neck mass (n=2) or enlarged lymph node (n=1).

Overweight

Height and weight at diagnosis were obtained for each case ≥ age 18 years from thyroid surgery anesthesiology records and used to calculate values of body mass index (BMI = kg/m2). Cases were then categorized according to National Center for Health Statistics criteria as "overweight" for BMI ≥27.8 in adult males and ≥27.3 in adult females, and "severely overweight" for BMI ≥31.1 in adult males and ≥32.3 in adult females. Table 11 gives the distribution of bodyweight classification by sex and time period for the LAC case series. The data show that a much higher percentage (58%) of the 1988-1995 female cases were either overweight or severely overweight compared to the 1970-1987 female cases (19%) and all male cases (13%). None of the females were known to be pregnant at surgery. One female was six months post-partum at surgery.

Table 11
Distribution of Bodyweight Classification by Sex and Time Period of Diagnosis for Los Alamos County Thyroid Cancer Cases ≥18 Years of Age at Diagnosis, 1970-1995

	Males		Females	
Bodyweight classification	1970-1987	1988-1995	1970-1987	1988-1995
Not overweight	2 (67)	11 (92)	13 (81)	8 (42)
Overweight	0 (0)	1 (8)	1 (7)	7 (37)
Severely overweight	1 (33)	0 (0)	2 (12)	4 (21)
Total	3 (100)	12 (100)	16 (100)	16 (100)

Examination of the female BMI data by age showed that the excess prevalence of overweight among the 1988-1995 female cases was localized to women < 50 years of age at diagnosis. Among these women, nine of 13 (69%) were overweight at diagnosis, and four (31%) were severely overweight. In comparison, two of 11 (18%) 1970-1987 female cases were overweight, and one (9%) was severely overweight. Among the cases ≥50 years of age at diagnosis during 1970-1987 and 1988-1995, 20% and 33% were respectively overweight.

County residence characteristics

Data on select county residence characteristics were obtained from information abstracted from LAMC patient medical charts. Estimated year of entry into LAC was based on either direct reference within the medical chart (43%) or from the date of the first LAMC outpatient medical record entry (57%). Estimated duration of county residence prior to diagnosis was calculated as the number of years elapsed between the year of entry into the county and the year of diagnosis. Table 12 gives a distribution of estimated year of entry into LAC by sex and time period. No particularly unusual trend was observed. The data show that the 1970-1987 cases tended to enter the county earlier than the 1988-1995 cases, particularly the female cases. Among the 1988-1995 cases, the temporal pattern of migration into the county for both males and females was distributed roughly symmetrically with a peak during the 1970's. Thirteen percent (4/31) of the 1988-1995 cases had entered the county prior to 1960, 26% (8/31) during the 1960's, 35% during the 1970's, and 26% after 1980.

Table 12
Distribution of Estimated Year of Entry into County by Sex and Time Period of Diagnosis for Los Alamos County Clinical Thyroid Cancer Case Series, 1970-1995

	Males		Females	
Year of entry	1970-1987	1988-1995	1970-1987	1988-1995
1943-1949	-	-	2 (11)	-
1950-1959	-	2 (17)	5 (28)	2 (11)
1960-1969	1 (25)	3 (25)	5 (28)	5 (26)
1970-1979	3 (75)	4 (33)	5 (28)	7 (37)
1980-1989	-	1 (8)	1 (5)	2 (11)
1990-1993	-	2 (17)	-	3 (16)
Total	4 (100)	12 (100)	18 (100)	19 (100)

Table 13 gives a distribution of estimated duration of residence in LAC prior to diagnosis by sex and time period. Nearly 20% of the male and female cases diagnosed during 1988-1995 had moved to LAC within two years of diagnosis. A lower percentage (14%) was seen for the 1970-1987 cases. Roughly half (48%) of the 1988-1995 cases had lived in the county in excess of 20 years prior to diagnosis, whereas relatively few had resided in the county between two and nine years prior to diagnosis. Ten of the total 53 clinical cases had resided in LAC during childhood. Age at entry into the county for these cases ranged from zero (born in LAC) to five years. Six were diagnosed in 1970-1987 (five females, one male) and four in 1988-1995 (two males, two females). The age at diagnosis ranged from six years to 35 years for the 1970-1987 cases, and 19 years to 30 years for the 1988-1995 cases.

Table 13
Distribution of Estimated Duration of Residence in County Prior to Diagnosis by Sex and Time Period of Diagnosis for Los Alamos County Clinical Thyroid Cancer Case Series, 1970-1995

	Males		Females	
Duration of residence	1970-1987	1988-1995	1970-1987	1988-1995
< 2 years	1 (25)	2 (17)	2 (11)	4 (21)
2-9 years	2 (50)	1 (8)	4 (22)	-
10-19 years	1 (25)	2 (17)	4 (22)	7 (37)
20+ years	-	7 (58)	8 (45)	8 (42)
Total	4 (100)	12 (100)	18 (100)	19 (100)

Summary

Table 14 gives a distribution of select etiologically-relevant attributes present among the LAC clinical case series by sex and time period. Although some cases displayed more than one attribute, each case was eligible to be entered only once into the table. Priority was given to the attributes as they are listed in the table. Overall, males expressed a much higher prevalence of attributes than females within either time period. Twelve of 15 (80%) male cases displayed one or more of the attributes compared to nine of 34 (26%) females. Of particular note was the absence of medullary carcinoma in females, the larger percentage of male cases (20%) compared to female case (3%) with a history of therapeutic irradiation of the head and neck, and the larger percentage of male cases (13%) compared to female cases (3%) with an occupational radiation exposure history. Among the 1988-1995 cases, 10 of 11 (91%) male cases displayed one or more attributes compared to five of 16 (31%) female cases.

Table 14
Distribution of Select Etiologically-Relevant Case Attributes by Sex and Time Period of Diagnosis for Los Alamos County Clinical Thyroid Cancer Case Series, 1970-1995

	Males		Females	
Case Attribute	1970-1987	1988-1995	1970-1987	1988-1995
Medullary carcinoma	1 (25)	2 (17)	-	-
Medical X-ray to head/neck	1 (25)	2 (17)	1 (6)	-
Resident < 2 years prior to diagnosis	-	2 (17)	2 (11)	4 (21)
Occupational radiation exposure	-	2 (17)	-	1 (5)
Parent had thyroid surgery for nodules	-	1 (8)	-	1 (5)
Incidental diagnosis of occult carcinoma	-	1 (8)	3 (17)	-
None of the above	2 (50)	2 (18)	12 (67)	13 (69)
Total	4 (100)	12 (100)	18 (100)	19 (100)

DISCUSSION

The epidemiologic investigation described in this report was conducted to document in detail the recent large excess of thyroid cancer in LAC and to explore possible causes. The analysis combined descriptive epidemiologic data along with clinical and risk factor data obtained from a case-series records review. The incidence of thyroid cancer in LAC has now been monitored up through 1995, and at present, appears to be declining from a peak excess centered within the years 1988 to 1993.

Rate Instability

The recent fourfold excess of thyroid cancer in LAC did not occur simply through instability in an incidence rate based on small case numbers. If thyroid cancer incidence rates for New Mexico had prevailed in LAC between 1988 and 1995, one would have expected about eight cases compared to the 31 cases observed. Thus, an excess of 23 cases occurred. When the LAC rates were compared to the state, a statistically-elevated incidence was observed during 1988-1995 for the entire county and for each sex. The 1988-1995 incidence in LAC also was close to being statistically-elevated over that observed among county residents during the preceding 18-year time period 1970-1987. Review of incidence rate data for five time periods between 1970 and 1992 showed that the rate of 20 per 100,000 observed in LAC was an unprecedented observation among New Mexico counties. Only two other county rates ever exceeded a rate of 15 per 100,000, of which both were based on two cases.

Detection artifact

The analysis presented in this report found little evidence to implicate a change in thyroid cancer detection as a cause of the recent excess. Active screening for thyroid cancer did not occur at any time between 1970 and 1995, nor did any significant change occur in disease detection methods. Palpation of an asymptomatic neck mass remained the predominant method of detection over the entire 26-year study time period. Although a shift toward more practitioner-detected tumors would have suggested an enhanced detection effect, virtually no change in the percentage of cancers detected by patients or by medical personnel occurred over the study time period. The majority of thyroid cancers (78%) were found by medical personnel, all of whom were practicing at the LAMC or the Laboratory at the time of discovery. No evidence was found implicating the introduction of a new health care practitioner into the local community with the excess.

Another possible explanation for the excess was that a greater overall awareness of thyroid cancer existed in LAC in recent times. It had been suggested that the Chernobyl accident, which occurred in April of 1986, may have caused an increased awareness which resulted in increased numbers of recent diagnoses. If such was the case one might have expected to see a trend toward smaller, less advanced tumors among cases diagnosed during recent times. This was not observed. A review of the pathologic characteristics of the thyroid cancers diagnosed during the early and later time periods failed to reveal any obvious difference in the extent of disease at diagnosis. It is possible, however, that a reservoir of undiagnosed clinical disease exists in the general population. This seems particularly likely for thyroid cancer given the indolent nature of the disease. Thus, one could hypothesize that a "harvesting" of cases in LAC might not necessarily be accompanied by an obvious shift toward less advanced tumors. The finding that nearly all of the LAC tumors were detected by palpation, a relatively insensitive technique for detecting small sub-clinical cancers, would be consistent with this hypothesis.

It had also been suggested that the thyroid cancer excess was simply a chance occurrence within an affluent population under close medical scrutiny. LAC residents actually may be near the extreme in regards to close medical surveillance given that a 53-bed community hospital was built by the U.S. government in 1950 specifically to meet the medical needs of the community. Moreover, the Laboratory provides an additional level of medical surveillance through it's occupational medicine program. The finding that 40% of all adult male clinical cases were detected at the Laboratory clearly demonstrates an impact from occupational health surveillance. Thus, LAC residents simply may be at higher risk of being diagnosed with thyroid cancer than residents of other communities. The finding that nearly 20% of the 1988-1995 cases had been diagnosed shortly after moving into the county provides some support for this premise.

Diagnosis Artifact

The investigation found little evidence to support changes in the diagnosis of thyroid cancer as a major cause of the recent excess. Virtually all patients in the LAC case series received a histologically-confirmed diagnosis following surgical biopsy, and most received their diagnosis at the LAMC. Although pathology reports were not reviewed for diagnostic accuracy, little reason exists to believe that a significant number of recent cancers would be reclassified as benign. The pathologic diagnosis of thyroid cancer from surgical specimens is relatively straightforward, except in the case of follicular carcinoma where definitive angioinvasion must be demonstrated. However, since only two follicular carcinomas were diagnosed among recent cases, reclassification of both to benign lesions would have little substantive effect on the observed excess. Another possible explanation was that more careful histopathologic examination in recent times had resulted in greater numbers of incidental diagnoses of small occult carcinomas. However, only one of 31 (3%) cases diagnosed between 1988 and 1995 involved an occult carcinoma. The percentage of incidental diagnoses actually was higher during the early time period 1970-1987.

Etiologic Considerations

Review of the descriptive epidemiology of thyroid cancer in LAC yielded a sharp pattern of contrasts between males and females. Such discrepancies tend to disfavor a common etiology. For example, LAC males experienced an unprecedented fivefold excess of thyroid cancer during 1988-1995 which was distinguishable not only by its magnitude and rapidity of onset, but also by a broad age distribution and a heterogenous mix of cell types, including two rarely diagnosed histologic forms. In contrast, the recent excess incidence observed in females was localized primarily to women between the ages of 30 and 59 years, was preceded by a elevated background incidence similarly localized to women in this age range, and was distinguishable by a near exclusive involvement of one histologic cell type.

The marked gender difference which characterized the descriptive epidemiologic analysis also was found to exist with the case-series review data. Again, such differences would tend to disfavor a common etiologic origin. For example, half of the 1988-1995 male cases involved patients who had been diagnosed with medullary carcinoma (n=2), had received therapeutic irradiation to the head and neck (n=2), or had recently moved into the county without any apparent risk factors (n=2). Of the remaining six cases, two had apparently received significant occupational exposures to ionizing radiation, one carried a positive paternal history of thyroid surgery for nodular disease, and one involved an incidental diagnosis of a small, occult papillary carcinoma. Thus, only two of the twelve (18%) male cases diagnosed during 1988-1995 were found to be absent of attributes either explanatory to an extent for thyroid cancer or exclusionary for a possible local exposure. In contrast, a majority (69%) of female cases were found to be absent of such attributes.

Obvious differential patterns of employment were observed between male and female cases. Working-age females were by and large employed in positions which typically do not involve radiological or chemical exposures. All of the males, however, were employed in positions with potential for exposure to toxicants. The finding that a relatively greater percentage of male cases had a positive history for occupational radiation exposure is consistent with the observed occupational data. The finding also is consistent with the longstanding male predominance in employment both within the nuclear industry and at the Laboratory in particular.

Several important differences were observed among females which tend to etiologically distinguish cases diagnosed during the early and later time period. One attribute which clearly distinguished the later female cases was the high prevalence of antecedent breast cancer. Three of 19 (16%) 1988-1995 cases had been diagnosed with breast cancer compared to none of the early cases. This finding may simply reflect closer medical surveillance of cancer patients, or alternatively, may signal some concordance in risk factors for the two diseases. In this regard, it is interesting to note that recent increases in the incidence of both breast and thyroid cancer have been observed among LAC women. It is also interesting to note that recent increases in endometrial cancer similarly have been observed in LAC. All three of these cancers are thought to be associated with overweight, an attribute which was found to be particularly prevalent among the 1988-1995 thyroid cancer cases. These findings suggest that an increasing prevalence in underlying host risk factors, such as overweight, could possibly be contributing to the recent increase in thyroid cancer observed among female residents of the county.

Local environmental hazards

Finding an elevated cancer rate within a geographically-defined area, such as a county or town, invariably raises a concern that the excess cases were caused by environmental hazards. Unfortunately, the complex multi-factorial etiology of most forms of cancer rarely permits a clear-cut response to such concerns. Moreover, since it is infrequent that data exist with which to accurately measure past exposures, if in fact a specific exposure is identified, rigorous studies usually cannot be designed to measure the level of risk. Compounding all this is the understanding that a community-based series of cancer cases usually includes individuals who differ by length of residence in the area. Thus, given the average latency period of two to four decades for many cancers, it is obvious that only a certain portion of the observed cases could be etiologically-linked to a putative local carcinogenic exposure.

All of the above conditions exist with the thyroid cancer excess recently observed in LAC. Here the public concern centered on potential excess ionizing radiation exposures related to Laboratory operations. Since ionizing radiation is a known cause of thyroid cancer, biologic plausibility certainly existed for the concern. Beyond this, however, little information existed with which to formulate a study hypothesis, much less assign exposure levels or doses. Consequently, the present investigation was undertaken to examine the excess in more detail to look for factors which either suggested a common etiologic link, or conversely, indicated distinguishing etiologic attributes. The results of the investigation supported the later scenario. Some cases could be explained on the basis of established risk factors, such as genetic susceptibility or medical irradiation, whereas other cases displayed attributes considered suspect risk factors, such as occupational radiation exposure, family history of nodular thyroid disease, and overweight. A number of cases displayed no apparent risk factors for thyroid cancer. Based on these findings, it can be reasonably concluded that environmental exposures likely did not singularly cause the recent excess.

A more quantitative perspective can be gained by consideration of several etiologic points. The first is that radiogenic thyroid cancer is thought to arise exclusively from follicular epithelial cells, particularly in the form of papillary carcinoma. Medullary carcinoma, a malignancy of the thyroid C-cells, is not believed to be induced by radiation. Two of the 31 (6%) cases diagnosed during the recent time period were medullary carcinomas. Given the absence of an etiologic link between ionizing radiation and medullary carcinoma, it seems reasonable to exclude these two cases from any hypothetical scenario involving excess environmental radiation exposures in LAC.

The second point relates to the issue of latency, the period of time intervening between exposure to carcinogens and diagnosis of disease. The latency period for radiogenic thyroid cancer in adults is estimated to be on the order of two to four decades. Individual latency periods likely vary depending on a number of determinants, including type of radiation, dose, dose rate, and age at exposure. Among the cases comprising the recent excess in LAC, all were adults at diagnosis, and six were known to have resided in the county less than two years prior to diagnosis. Given the slow-growing nature of most thyroid cancers, it is likely that these six individuals moved into LAC with their cancers. It thus seems reasonable to conclude that these six cases cannot be etiologically linked to putative carcinogenic exposure in LAC.

Of the remaining 23 cases, two had a history of therapeutic irradiation of the head and neck for benign conditions, a well-established risk factor for thyroid cancer. Although the presence of this risk factor does not necessarily rule out a role for environmental exposures, it seems reasonable to conclude that these cases more than likely were caused by medical radiation.

Based on the above considerations, it can be concluded that only 21 of the 31 (67%) 1988-1995 LAC thyroid cancer cases could potentially have been caused by an environmental radiation exposure in LAC. Any further dissection of the case series requires assumptive conditions. For example, if excess risk from a hypothetical environmental radiation exposure in LAC is conditional upon exposure in childhood (0-14 years), then no more than four of the 31 (13%) 1998-1995 cases could be attributed to the exposure. Alternatively, if a potential causal environmental exposure occurred in the 1950's or 1960's, then no more than 10 of the 31 (32%) recent cases could be implicated since the remaining cases had not yet moved into the county.

Strengths and Limitations of the Investigation

LAC is a unique community by many different measures, including the near exclusive delivery of routine health care services through the local community hospital. Virtually all local physicians have been located at the LAMC, which since inception has maintained a centralized medical records system. The major strength of the investigation was that nearly all study data were collected through the centralized medical records maintained at the LAMC. Since only a modest turnover in local physicians and surgeons has occurred over the past two decades, a remarkable level of consistency was found across the records. Moreover, each record was found to harbor a high level of detailed information concerning the detection and diagnosis of thyroid cancer, even if the case had been diagnosed out-of-county. This attention to detail is consistent with what might be expected for an affluent and closely-knit community such as that in LAC. These qualities also provided a level of assurance that other data items, such as estimated entry into the county and typical occupation, were reported with relative accuracy.

The major limitation to the investigation was that a medical records review by nature is an exploratory, hypothesis-generating exercise rather than an analytical study of causation. Thus, the results cannot be used to measure risk, which is usually the main desire of communities identified as having a high cancer rate. Since thyroid cancer likely has different causes, the approach employed here simply allows one to make an informed judgment based on those attributes and factors which were available for study.

RECOMMENDATIONS

The epidemiologic investigation described in this report did not identify a specific cause for the unusually high number of recent thyroid cancers in LAC. The likelihood is that the recent excess had multiple causes, some of which have been examined in this study, and some of which may never be identified. This has been the general experience of investigations of excess cancer in communities across the nation. By and large, the policy developed to deal with these issues has been to monitor locations where excesses have occurred, look for further clues among additional cases, and reevaluate new data if it becomes available. It is this policy which is recommended here. Surveillance data collected for 1994 and 1995 already have suggested that the fourfold peak excess which began in the late-1980's in LAC is now declining.

- Continue to monitor the incidence of thyroid cancer in LAC using cancer case data routinely collected by the NMTR.

- Continue to abstract and analyze epidemiologic and clinical information from the medical records of newly diagnosed cases of thyroid cancer in LAC.

- Re-evaluate the case information collected through the records review if indicated by new information on environmental exposures or other risk factors.

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Figure 1

Frequency Distribution of Newly Diagnosed Cases of Thyroid Cancer in Los Alamos County, 1970-1995

By Sex and Year of Diagnosis

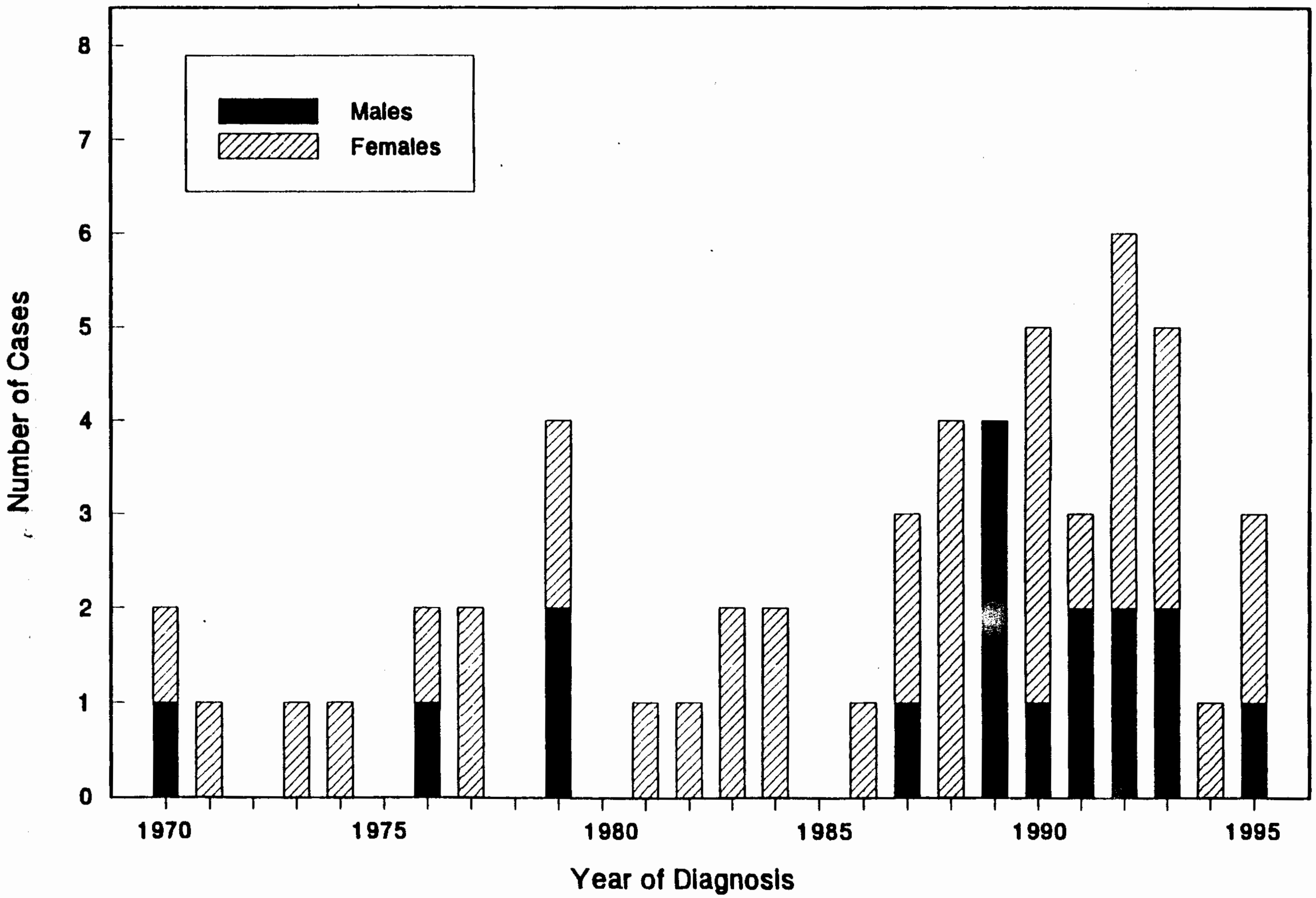
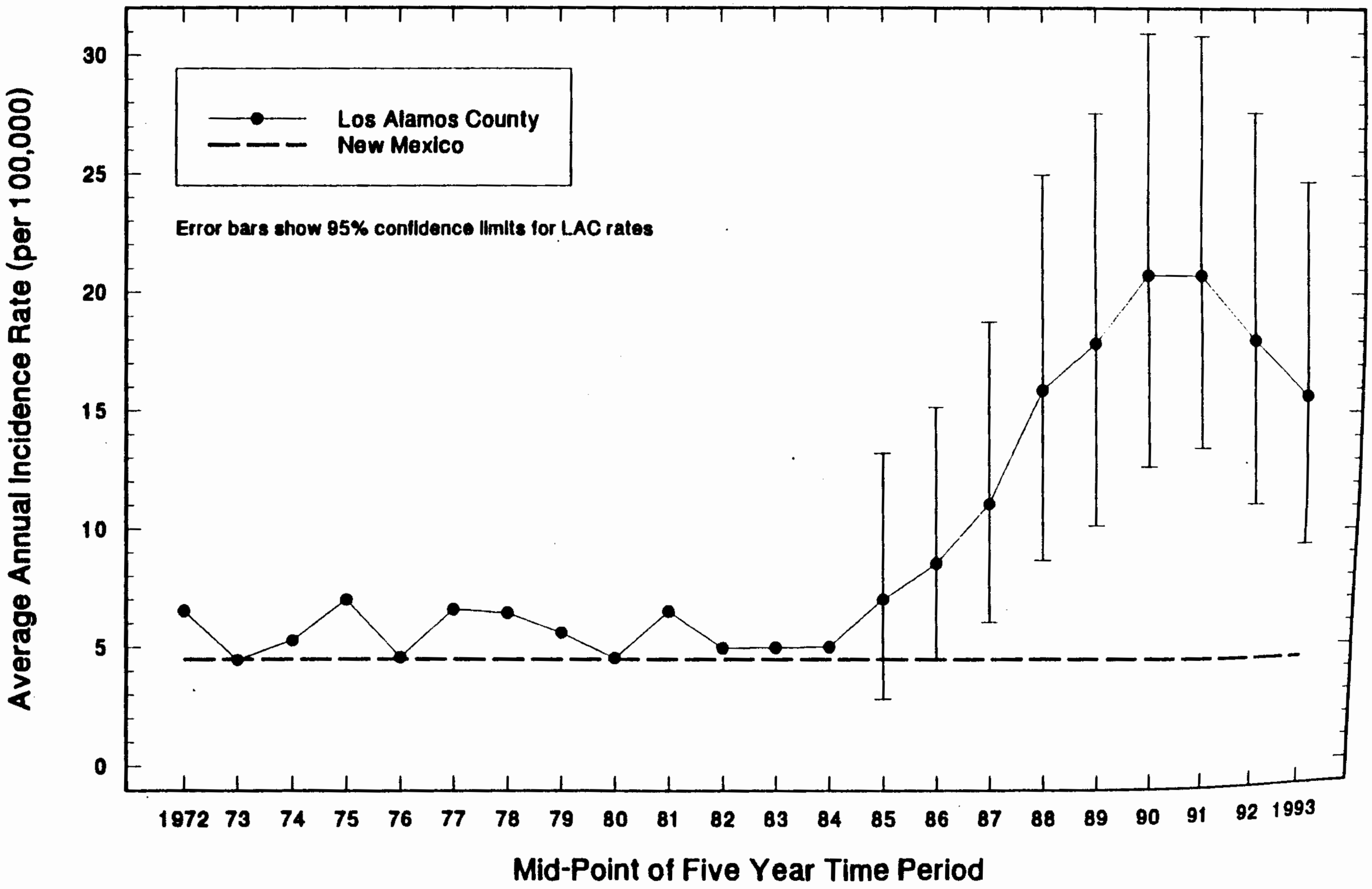


Figure 2

Age-Adjusted Incidence of Thyroid Cancer in Los Alamos County and New Mexico*, All Races, Both Sexes, 1970-1995

By Five-Year Moving Average Time Period



* Aggregate 1970-1992 New Mexico rate plotted

Figure 3

Age-Adjusted Incidence of Thyroid Cancer in Los Alamos County and Neighboring Counties, All Races, Both Sexes, 1970-1992

By Time Period and County

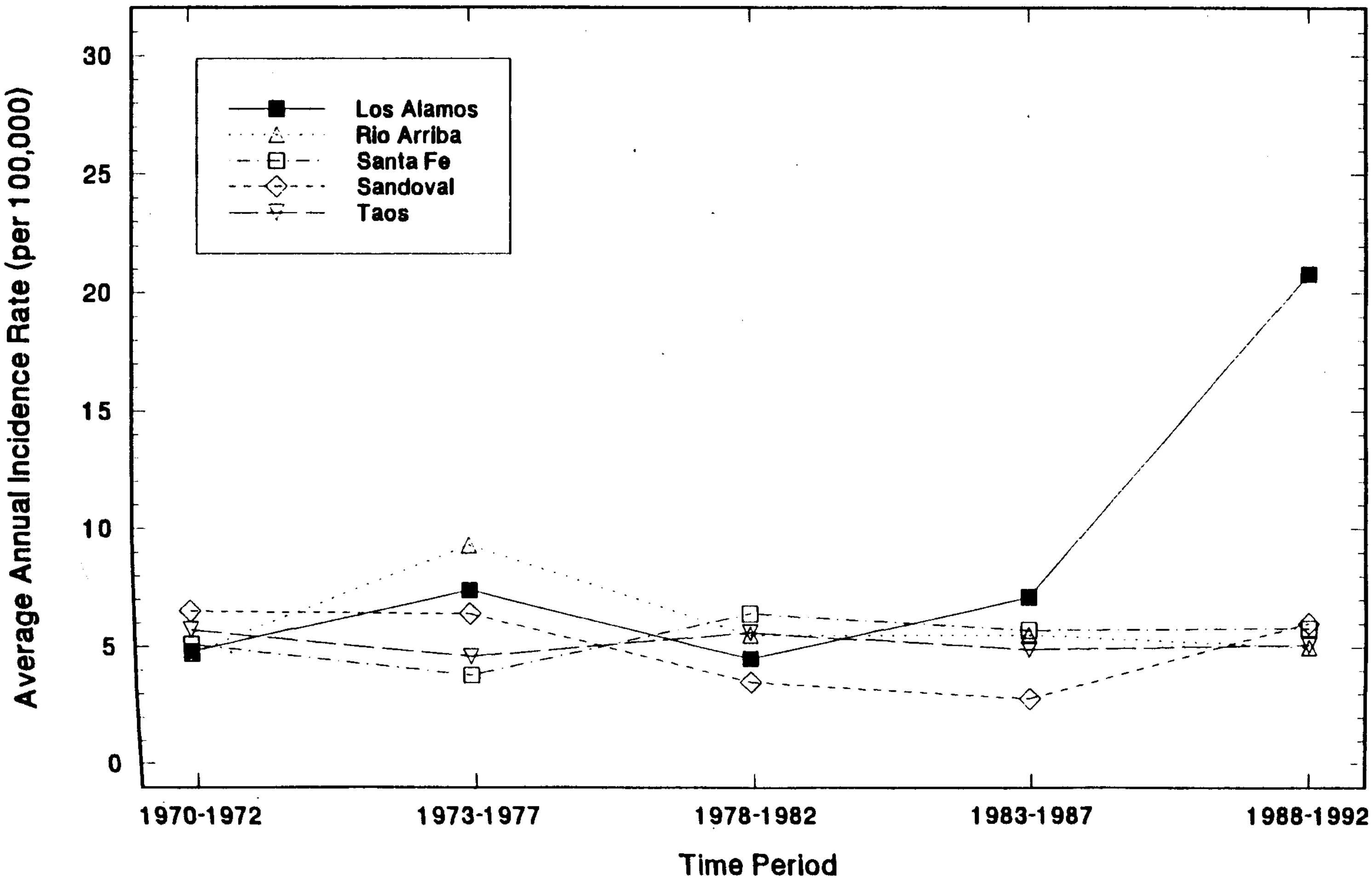
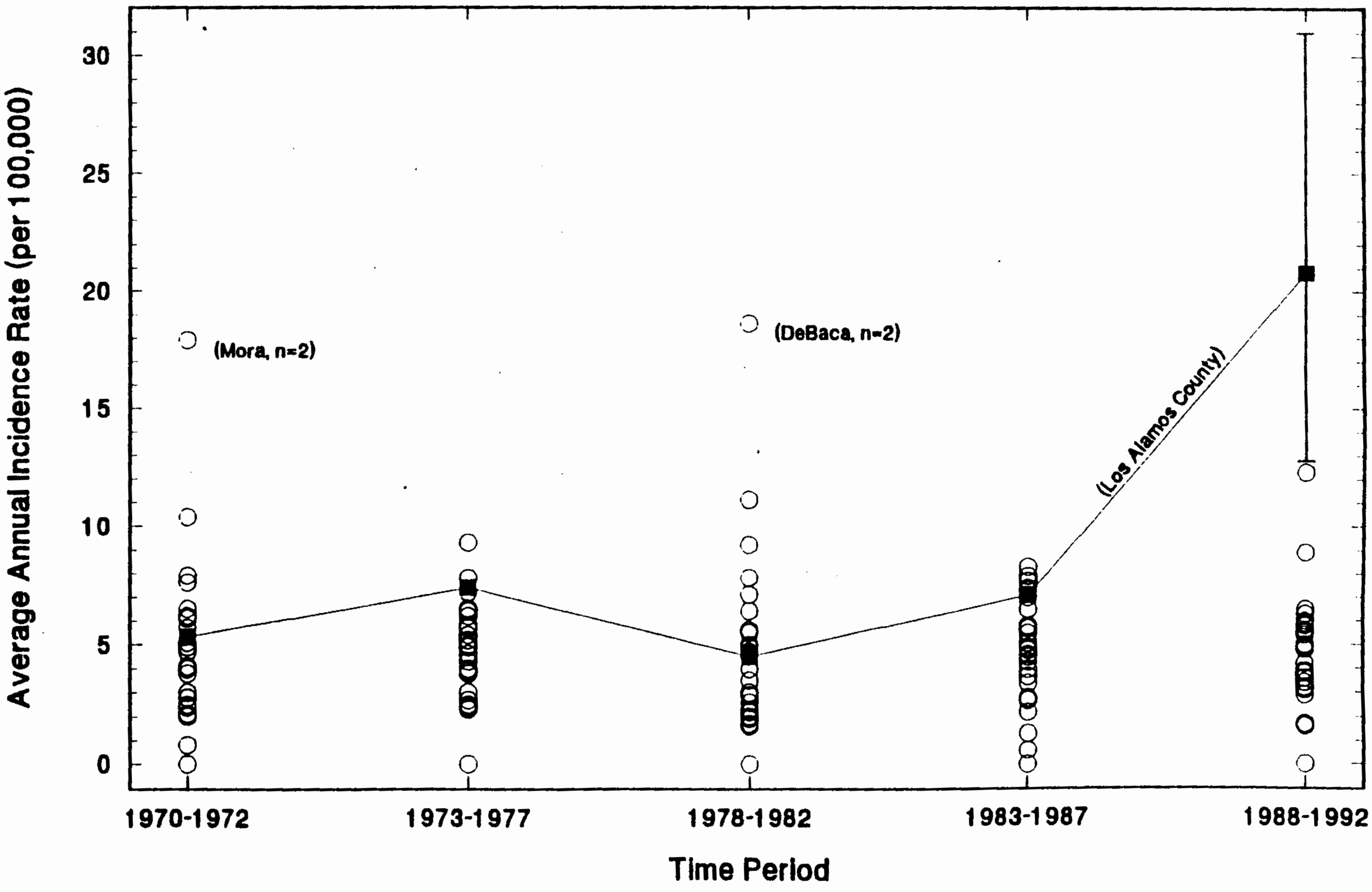


Figure 4

Scatter Plot of Age-Adjusted Thyroid Cancer Incidence in New Mexico Counties, All Races, Both Sexes, 1970-1992

By Time Period

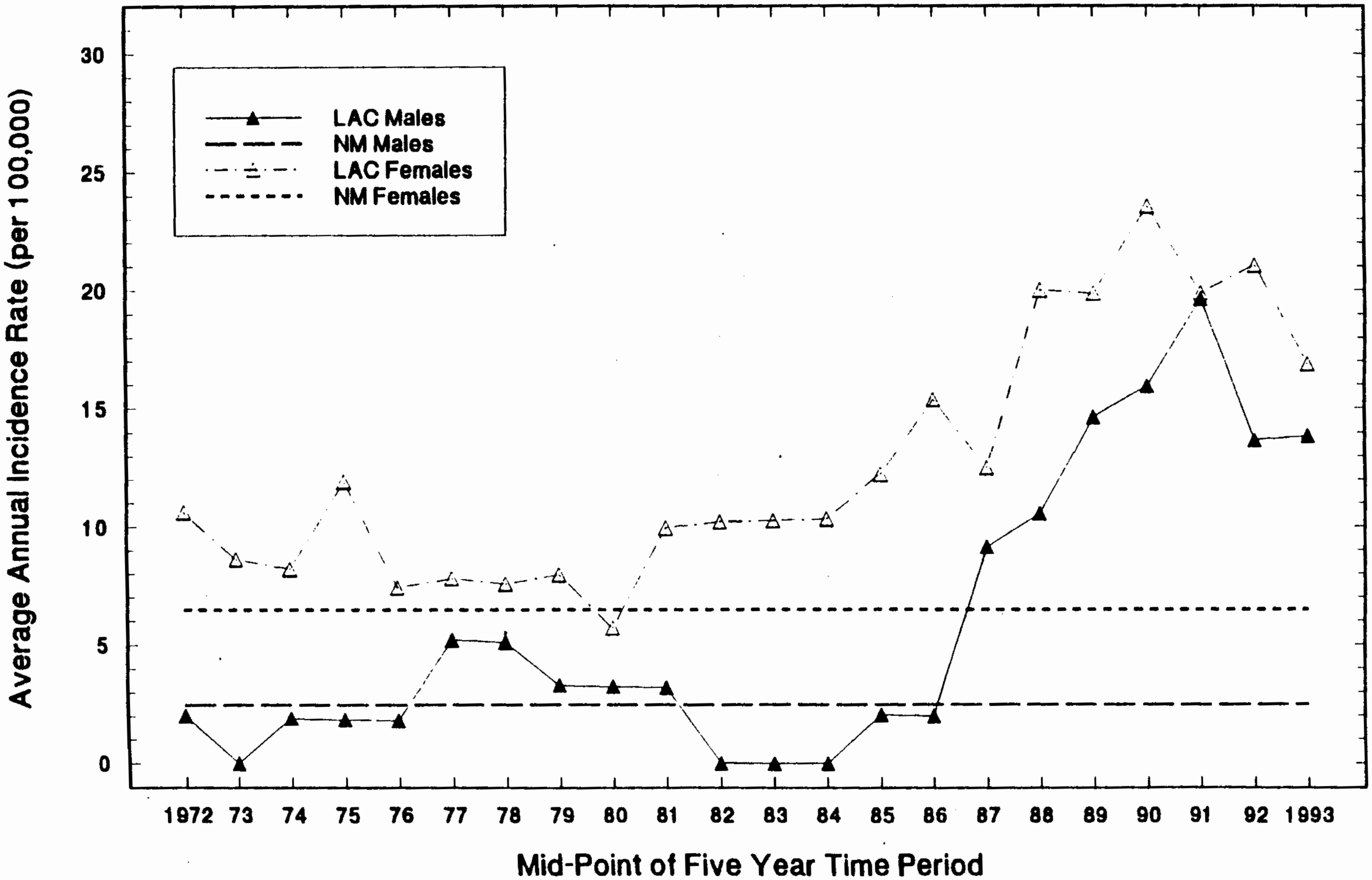


Error bars show 95% confidence interval

Figure 5

Age-Adjusted Incidence of Thyroid Cancer in Los Alamos County (LAC) and New Mexico* (NM), All Races, Males and Females, 1970-1995

By Sex and Five-Year Moving Average Time Period



* Aggregate 1970-1992 New Mexico rate plotted

Figure 6
Age-Specific Incidence of Thyroid Cancer in Los Alamos County and New Mexico, All Races, Males, 1970-1995

By Time Period

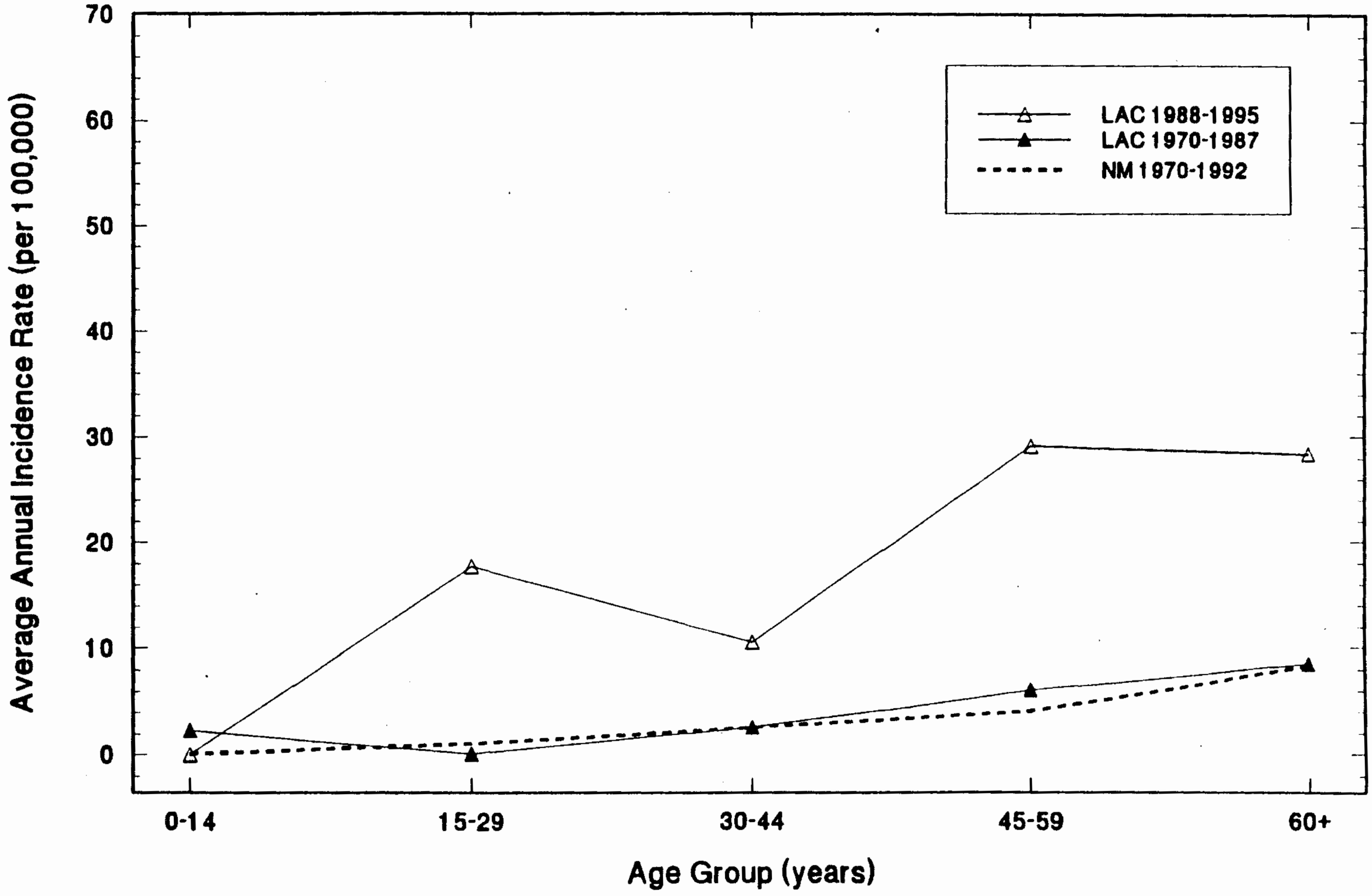


Figure 7
Age-Specific Incidence of Thyroid Cancer in Los Alamos County and New Mexico, All Races, Females, 1970-1995

By Time Period