THE UNIVERSITY OF OKLAHOMA

GRADUATE COLLEGE

MORTALITY AMONG FEMALES EMPLOYED BY THE LOS ALAMOS NATIONAL LABORATORY: AN EPIDEMIOLOGIC INVESTIGATION

A DISSERTATION

SUBMITTED TO THE GRADUATE FACULTY

in partial fulfillment of the requirements for the

degree of

DOCTOR OF PHILOSOPHY

BY

LAURIE DIANE WIGGS

OKLAHOMA CITY, OKLAHOMA

1987

cop. 2

MORTALITY AMONG FEMALES EMPLOYED BY

THE LOS ALAMOS NATIONAL LABORATORY:

AN EPIDEMIOLOGIC INVESTIGATION

APPROVED BY

[redacted]

DISSERTATION COMMITTEE

ACKNOWLEDGEMENTS

I would like to thank the members of my committee, Elisa T. Lee, Stanley L. Silberg, Willis L. Owen, Gregory Istre, and Charles Lawrence, for their patience and guidance during this process. I would especially like to thank my advisor and committee chairman, Dr. Elisa T. Lee. I also acknowledge the assistance and support given me by my late advisor, Dr. Paul S. Anderson.

I wish to thank the Department of Energy project officer, Dr. Robert Goldsmith, who provided funding for the Plutonium Workers Study. I also wish to thank a number of persons at Los Alamos for their assistance and support. I would like to thank Gregg S. Wilkinson for allocating the personnel resources to make the project possible. I also wish to thank the following Laboratory managers for their support and guidance during this process: George L. Voelz, M.D. and William H. Greendyke, M.D. I especially want to thank Carol Weber for her extensive programming and analytic support. I thank B. Joan Essington for her data entry, typing, and moral support. I also wish to thank Adelaide Fu for her clever tracing techniques, without which many of these subjects would not have been located. I thank Annabelle Salazar and Warren Galke for their efforts in preparing the final document.

Finally, I would like to thank Jesse Aragon, Health, Safety and Environment Division Leader, for making it possible for me to further my graduate education.

I especially wish to thank my family for standing behind me. I would like to thank my mother and late father for giving me the opportunity, and more importantly, the desire to obtain a good education. My father told me that an education was the only thing he could give me that no one could ever take away. My mother continued to support me in this belief after my father's death. She encouraged me to continue my education and made it possible for me to do so. I would like to thank my brother John, my cousin Melba, and my Auntie Bon for believing in me. I benefited enormously from their encouragement. Finally, I would like to thank my husband Ronald Scripsick for living with me through this ordeal and for sticking by me when I returned to school.

Work performed at the Los Alamos National Laboratory under the auspices of the US Department of Energy under contract W-7405-ENG-36.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF ILLUSTRATIONS

MORTALITY AMONG FEMALES EMPLOYED BY THE LOS ALAMOS NATIONAL LABORATORY: AN EPIDEMIOLOGIC INVESTIGATION

CHAPTER I

INTRODUCTION

The Los Alamos National Laboratory, formerly the Los Alamos Scientific Laboratory, began operations in 1943 as part of the Manhattan Engineering District (MED) Project.

The purpose of the World War II MED was to develop the world's first atomic bomb. The Manhattan Project included nuclear research facilities at the Crocker Radiation Laboratory (Berkeley, California), the Clinton Laboratory (Oak Ridge, Tennessee), the Chicago Metallurgical Laboratory (Chicago, Illinois), the Dayton Laboratory (Dayton, Ohio), the Hanford Works (Richland, Washington), and Project Y (Los Alamos, New Mexico) (Department of Energy, 1979). The purpose of Project Y, the wartime predecessor of the Los Alamos National Laboratory, was to design and build the first atomic bomb. This secret laboratory was established in New Mexico at the site of a private boys school, the Los Alamos Ranch School, which was condemned by the War Department for this project. Project Y grew from a few scientists in early 1943 to a community of more than 5000 scientists and support personnel in 1945 (Kunetka, 1979).

During those two years, Project Y, under the direction of Dr. J. Robert Oppenheimer, designed and built two types of atomic bombs. The uranium gun bomb functioned by firing one subcritical piece of uranium into another, resulting in an explosion. The uranium bomb was nicknamed "Little Boy". The other type of bomb, nicknamed "Fat Man", was a plutonium implosion bomb. This bomb functioned by surrounding a subcritical mass of plutonium with high explosives, which when detonated compressed the plutonium into a critical mass that exploded.

Project Y fulfilled its mission with the detonation of the "Fat Man" bomb at the Trinity Test Site, near Alamorgordo, New Mexico, on July 16, 1945 (Kunetka, 1979).

After World War II, the Los Alamos Laboratory continued research in the areas of nuclear weapons development and the peaceful uses of nuclear energy. Research areas eventually expanded to include a variety of areas including mathematics, physical science, environmental and health sciences, and energy research (Department of Energy, 1979).

This reports a study of mortality among female employees of the Los Alamos National Laboratory from 1943 to 1981. This study examined the possible relationship between radiation exposure and cancer mortality.

CHAPTER II

LITERATURE REVIEW

Studies of persons exposed to external ionizing radiation have suggested that there are observable health effects at high doses of radiation exposure. Examples of these health effects include studies of the atomic bomb survivors and studies of individuals exposed to clinical or therapeutic radiation. Recently, studies of workers in the nuclear industry have examined individuals exposed to much lower levels of radiation exposure, which have usually been received over a protracted period of time in the work setting. Studies of these nuclear workers include recently published results among nuclear shipyard workers, results among workers at the DOE facilities of Hanford, Rocky Flats, Lawrence Livermore, and Oak Ridge, and results of studies among two cohorts of British nuclear workers.

Studies of cancer mortality and incidence among atomic bomb survivors, among persons exposed to clinical and therapeutic radiation, among occupationally exposed workers in the nuclear industry, and previously completed studies of Los Alamos workers will be reviewed.

Studies of Atomic Bomb Survivors

Survivors of the atomic bombs dropped on Hiroshima and Nagasaki, Japan in 1945, have been extensively followed since approximately 1950, when the life span study (LSS) was initiated. In 1978, Beebe et al. (1978) reported on the mortality experience of atomic bomb survivors from 1950 through 1974. Beebe et al. (1978) reported that "in addition to leukemia and cancer of the thyroid, breast, and lung, now cancer of the esophagus, stomach, and urinary organs, and the lymphomas, should be included among the forms of cancer caused by ionizing radiation from the 1945 atomic explosions." Leukemia appeared much earlier in the atomic bomb survivors than other malignant neoplasms. Leukemia incidence has declined with continued follow-up, while incidence at other malignant neoplasms has increased. Minimum latent periods for the development of cancer have been estimated to be less than 15 years, although these latent periods are influenced by the site of cancer under study (Beebe et al., 1978).

Wakabayashi et al. (1983) examined cancer incidence based on the data from the Nagasaki Tumor Registry. Statistically significant dose response relationships were observed for "all cancers, leukemia, all cancers except leukemia, and cancers of the stomach, colon, liver, lung, thyroid, breast (females only), prostate, urinary tract, and multiple myeloma."

Excess breast cancer has been reported among female atomic bomb survivors (McGregor et al., 1977; Tokunaga et al., 1979). Studies by McGregor et al. (1977) and Tokunaga et al. (1979) indicated that risk was highest for women irradiated before age 20, when breast tissue was most likely to be growing. A premenarche versus post menarche difference was not verified by the later study (Tokunaga et al., 1979). Both McGregor et al. (1977) and Tokunaga et al. (1979) reported that irradiation did not shorten the latency period for the development of breast cancer. Latency periods were comparable for irradiated women and their nonexposed controls. Latency periods for the development of breast cancer were estimated to be at least 10 years (Tokunaga et al., 1979).

Another interesting finding in the studies of atomic bomb survivors was the determination that thyroid cancer was more common among female than male survivors (Parker et al., 1974). The other notable finding from this study was that cancers of the thyroid were observed in persons up to the age of 50 at the time of irradiation, contrary to other evidence suggesting risk primarily during childhood.

It should be noted that the atomic bomb radiation dose estimates have been questioned and recalculated (Kopecky, 1987).

A presentation (Kopecky, 1987) at the Society for Epidemiologic Research's Twentieth Annual Meeting described the new radiation dose estimates (DS86) for the atomic bomb survivors. In general, the new dose estimates decreased compared with the T65 doses, that have been used in the health effects studies in the past. For Nagasaki, the gamma and neutron doses decreased by approximately the same amount. For Hiroshima, the neutron doses decreased considerably, while a crossover was observed for the gamma doses. The new Hiroshima gamma doses are higher than the T65 doses at higher dose levels and lower than the T65 doses at lower dose levels. With these changes in dose estimates, the differences between the cities have "largely" disappeared. Calculations made with an interim set of dose estimates

(I85D) suggest that the estimates of relative risk will increase when the new dose estimates are incorporated into the epidemiologic studies.

Studies of Persons Receiving Clinical/Therapeutic Radiation

A number of studies have been conducted among individuals exposed to radiation for diagnostic or therapeutic reasons. Doses received by these individuals were often quite large. Sometimes exposures consisted of a single course of treatment and sometimes included a number of treatments delivered over a prolonged time. Studies of persons given x-radiation treatments resulting in excess breast cancer, thyroid cancer, gynecological cancer, and cancer of heavily irradiated sites (ankylosing spondylitis) are described. In addition, studies of cancer among persons treated with the internal emitters of radium and thorotrast will be described.

Breast Cancer Among X-radiated Individuals

Elevated rates of breast cancer have been reported in many studies of women exposed for clinical or therapeutic reasons to high doses of ionizing radiation. Shore et al. (1977) reported that women whose breasts were irradiated to treat postpartum mastitis demonstrated an excess breast cancer incidence. This excess could not be accounted for by genetic factors, the presence of known breast cancer risk factors, or existing disease state. In women receiving unilateral irradiation, the excess was observed only in the breast that was irradiated.

Subsequent follow-up of the women irradiated for acute postpartum mastitis was reported in 1986 (Shore et al., 1986). A statistically significant relative risk of 3.2 (90% CI = 2.3, 4.3) was observed for irradiated breasts. Although a linear dose response relationship was observed, the risk decreased at very high doses. This may suggest a cell-killing effect at these high doses. Excess breast cancer was observed beginning at approximately 15 years after radiation, suggesting this was the minimal latent period for the development of breast cancer due to radiation in this group.

An excess of breast cancer incidence has also been reported for women who were exposed to fluoroscopic chest examinations during treatment for tuberculosis between 1930 and 1954 in two Massachusetts tuberculosis sanatoria. Boice and Monson (1977) observed 41 cases of breast cancer compared with 23.3 expected (p=0.0006). No significant excess of breast cancer cases was observed for nonirradiated comparison subjects (15 observed and 14.1 expected). The crude incidence rate for breast cancer was 15.1/1000 women-years for the exposed and 0.8/1000 women-years for the nonexposed.

Thyroid Neoplasms Among X-radiated Individuals

Ron and Modan (1980) have reported a significant excess of benign and malignant thyroid neoplasms among a cohort of 10,842 persons exposed in childhood to an average x-radiation dose of 9 rads for the treatment of tinea capitis. Incidence of thyroid tumors was three times higher in irradiated women compared with irradiated men. The authors suggested that a multiplicative model describes the relationship between sex and radiation exposure in the development of thyroid cancer.

Shore et al. (1976) reported a similar excess incidence of cancer of the thyroid among 2215 persons treated for tinea capititis with x-ray therapy during childhood. Estimated dose to the thyroid among members of the exposed group ranged from 4 to 8 rads. They reported that the crude incidence rate for cancer of the thyroid was 7.0/1000 among females and 2.1/1000 among males. In addition, Shore et al. (1976) reported an excess incidence of cancer of the brain among these irradiated subjects. They observed six brain tumors among the irradiated group while none were observed among the nonexposed controls (p=0.07).

Excess thyroid tumors have also been observed in a group of persons treated with x-rays for enlarged thymus glands during infancy (Shore et al., 1980; Shore et al., 1985). In the recent follow-up (Shore et al., 1985), irradiated subjects were compared with their nonirradiated sibling controls and the relative risk observed for malignant thyroid tumors was 49 (90% CI = 10.7, 225.0). A significant excess was also observed when the cases of thyroid cancer were compared with an expected value based on the rates for upstate New York. A relative risk of 15 (90% CI = 8.1, 27.7) was observed for benign thyroid adenomas. Among females, the risk of thyroid cancer was two to three times higher than among males (Shore et al., 1985).

Cancer Among Persons X-radiated for the Treatment of Ankylosing Spondylitis

Another large group of individuals treated with therapeutic radiation included patients suffering from the crippling disease, ankylosing spondylitis. Court Brown and Doll (1965) reported that patients treated with x-rays experienced excess mortality from leukemia, aplastic anemia, and cancers of sites that were "heavily irradiated" when compared with expected values based on rates for England and Wales. Cancers of "lightly irradiated" sites were not significantly increased. Subsequent follow-up (Smith and Doll, 1978) of these patients irradiated for the treatment of ankylosing spondylitis reported that the greatest increase in leukemia deaths occurred 3 to 5 years after irradiation, while the excess of cancers of the "heavily irradiated" sites peaked at approximately 10 years after irradiation. Overall mortality was 66% greater than expected based on rates for England and Wales. When the "heavily irradiated sites" were examined separately, the only significantly elevated cause-specific cancer was cancer of the central nervous system (spinal cord and nerves). The authors felt that an observed excess of colon cancer was most likely due to the effects of the disease (ankylosing spondylitis) rather than the treatment (radiation).

Cancer Among Women Receiving Gynecological Irradiation

A cohort of Connecticut women with benign gynecological conditions who were treated with x-rays or radium implants from 1935 through 1966 was identified. Among these women, 12 incident uterine sarcomas were identified compared with an expected incidence of 1.5 cases based on Connecticut Tumor Registry incidence data. Although observed in both the x-ray and radium treatment group, the excess of uterine sarcomas was greatest among the patients treated with radium implants. In addition, cancers of irradiated sites were observed for cancers of the female genital organs (109 observed compared with 54.9 expected), cancers of the kidney and bladder (17 observed compared with 8.5 expected) and lymphatic and hematopoietic cancers (27 observed compared with 11.9 expected). Twelve leukemias compared with 5.3 expected were also observed (Wagoner, 1984).

Bone Cancer Among Patients Treated With Radium

Radium, an alpha emitter similar to plutonium, has been used to treat patients for a variety of conditions including ankylosing spondylitis, bone tuberculosis, and other diseases. A cohort of 898 German patients treated with radium-224 demonstrated a large excess of bone sarcomas with 53 observed compared to an expected number of 0.2 based on the general population (Mays and Speiss, 1984).

Cancer Among Patients Administered Thorotrast

Thorotrast, thorium dioxide, was injected into patients to serve as an radiological contrast medium. Thorotrast was injected both systemically and locally, although local usage was considerably less common. Thorotrast is an internal emitter which is permanently retained in the human body (da Silva Horta et al., 1974).

Patients administered thorotrast in Portugal, Germany, and Denmark have been followed epidemiologically. A series of 2434 Portuguese administered thorotrast from 1930 to 1950, demonstrated elevated rates for cancers of the liver, bone, lung, and leukemias when compared both with a control series given a nonradioactive contrast medium and with expected values based on the Portuguese population (da Silva Horta et al., 1978).

A series of 6000 thorotrast-injected patients and 6000 hospital controls have been studied in Germany. Among deceased members of the study, 88 liver cancers were observed for thorotrast injected patients compared with 6 among members of the control group. Among thorotrast patients entered into a clinical examination program, high incidences of liver cancer and leukemias have been observed (van Kaick et al., 1978).

Among Danish thorotrast patients followed since 1949, clear excesses of liver cancers and leukemias have been observed. Some evidence of elevated rates for cancers of the bone and lung has been observed, although additional follow-up will be required to determine whether bone and lung cancer have been induced by the injection of thorotrast in this series of patients (Faber, 1978).

Studies of Persons Exposed to Radiation in the Occupational Setting

Uranium Miners and Millers

In 1964, Wagoner et al. (1964) reported excess mortality among white uranium miners working on the Colorado Plateau. They observed 218 deaths compared with 148.7 ($p < 0.01$) expected based on rates for male residents of the Colorado Plateau. A large excess of respiratory cancer was also observed with 15 cases compared to 4.2 expected ($p < 0.01$). A smaller excess of all malignant neoplasms (30 observed compared with 18.7 expected, $p < 0.05$) was observed among miners. Furthermore, these miners demonstrated high rates of injury deaths, many of which were associated with mining activities. When the cohort was divided into above-ground and underground miners, the significant excesses of deaths due to all cancers and respiratory cancers were observed only among underground miners. Excess injury deaths were observed for both subcohorts.

A subsequent study (Wagoner et al., 1965) examined mortality among 3415 underground uranium miners. Significant excesses were observed for all causes of death (249 observed compared with 153.2 expected), all cancers (41 observed compared with 21.3 expected), all respiratory cancer (22 observed compared with 5.7 expected) and all injury deaths (95 observed compared with 33.9 expected). Approximately 57% of the injury deaths occurred in the mines. Perhaps the most important result of this investigation was that Wagoner et al. (1965) demonstrated a strong dose-response between cumulative radiation exposure and the occurrence of respiratory cancer.

A recent paper (Saccomanno et al., 1986) reported results of studies of uranium miners on the Colorado Plateau. When the authors matched on smoking history and age, the risk of lung cancer in miners employed 11 or more years was 8.5 times the risk of lung cancer among nonminers. The risk of lung cancer among uranium miners was three times that of smokers in the general population.

Additional studies of uranium miners are also under way. In 1981, Chovil (1981) reported a "strong dose-response" between radiation and lung cancer incidence among Ontario uranium miners.

New Mexico uranium miners are currently being studied by researchers at the University of New Mexico. In a status report, Samet et al. (1983) stated that 276 deaths had been identified among a cohort of 3055 underground uranium miners. A total of 44 lung cancer deaths, 39 coded as lung cancer and 5 originally coded as carcinomatosis, were identified. Based on the 39 cases, the lung cancer proportional mortality among New Mexico miners (14%) was similar to the lung cancer proportional mortality (16%) among Colorado Plateau miners. Studies of this cohort are continuing. In 1986, Morgan and Samet (1986) published a detailed report describing the nature and level of cumulative radon-222 daughter exposures among the New Mexico miners.

A case-control study of Navajo men, who developed lung cancer, determined that 72% of the lung cancer cases in this group were attributable to employment as uranium miners. Navajos traditionally smoke less than whites and among Navajo lung cancer cases who smoked, the average consumption was only 2.3 cigarettes per day. The lower bound for the relative risk of lung cancer associated with uranium mining was 14.4. The point estimate for the relative risk could not be calculated because none of the controls had worked as uranium miners. This investigation demonstrated that uranium mining alone, without smoking, can increase the risk of lung cancer (Samet et al., 1984).

Wagoner et al. (1964) examined a cohort of uranium millers working on the Colorado Plateau and observed no excess mortality among these millers. A later study (Archer et al., 1973) of uranium millers, however, demonstrated an excess of deaths due to cancers of the lymphatic and hematopoietic system, excluding leukemias. Archer et al. (1973) observed 4 cases of lymphatic cancers compared with 1.02 expected ($p < 0.05$).

Radiologists

When mortality was examined for radiologists and other physician specialists, radiologists first employed before 1940 had an excess of all cause and all cancer mortality when compared with physicians practicing other medical specialties. A "dose-response" relationship was observed, whereby mortality rates paralleled theoretical radiation exposure levels for various physician specialties. Radiologists ranked first followed by internists, otolaryngologist and, finally, opthamalogists (Matanoski et al., 1975a). When mortality from specific cancers was observed, leukemia was elevated among radiologists first practicing before 1940 compared with physicians in other specialties. Leukemia rates for these radiologists first practicing before 1940 were also significantly greater than those expected based on US death rates. In addition, lymphoma death rates were also significantly greater than expected based on US rates for radiologists first practicing between 1930 and 1949 (Matanoski et al., 1975b).

Radium Dial Painters and Luminisers

During the 1920's a newly discovered form of "occupational poisoning" was described among individuals ingesting radium and mesothorium while painting luminous watch dials (Martland et al., 1925; Martland et al., 1929). The material was introduced into the body when workers "pointed" the brush with their lips.

Today, studies of US female radium dial painters are ongoing at the Center for Human Radiobiology at Argonne National Laboratory. In 1978, Polednak et al. (1978) reported mortality among a cohort of 634 women first employed between 1915 and 1929 in the US radium dial painting industry. Among these 634 women, a significant excess of mortality due to all causes of death (SMR = 127, p <0.001) was observed. Mortality from all cancers (SMR = 193), cancers of the colon (SMR = 202), cancers of the bone and mastoid cavity (SMR = 8179), other and unspecified cancer sites (SMR = 716), diseases of the blood and blood-forming organs (SMR = 391), and injuries (SMR = 308) was significantly elevated among these women.

Dose-response analyses were conducted for 300 women alive in 1954 and subsequently monitored to determine their radium exposure. Women who were monitored at autopsy or after exhumation were not included in these dose-response analyses. Significant excesses of mortality were observed in the high-dose category ($\geq$50 uCi) for all causes (SMR = 191), all cancers (SMR = 397), and other and unspecified neoplasms (SMR = 2273). Cancers of the bone and mastoid cavity were more than 225 times greater than expected among women in the high-dose category.

Only cancer of the colon was significantly elevated among women in the low-dose category (<50 uCi). No bone cancers were observed among low-dose women (Polednak et al., 1978). Although not calculated, direct estimates comparing the rates of disease among high-dose and low-dose women would be high. For example, a crude estimate of the ratio of all cancer mortality in high-dose women compared with low-dose women results in an unadjusted crude mortality density ratio of 3.36, while a crude mortality ratio of 22.42 would result for other and unspecified neoplasms. The estimate of the ratio for bone tumors would be undefined due to an absence of cases among the low-dose women.

Adams and Brues (1980) reported excess breast cancers (36 observed compared with 23.77 expected, $p < 0.05$) among radium dial painters first employed before 1930. When the cohort was divided into two groups, those for which an estimate of dosimetry was available (measured) and those for whom no estimate of dosimetry was available (unmeasured), only the unmeasured group demonstrated an excess of breast cancer mortality (mortality ratio = 3.38, $p < 0.001$). This result was not surprising and was most likely due to differential survival among measured and unmeasured members of the cohort because measured women must have survived until at least 1954 to have been measured. When the measured women were examined, women with intake doses of ≥ 50 uCi demonstrated significantly more breast cancer (mortality ratio = 5.8, $p < 0.001$) than expected.

Spiers et al. (1983) reported no excess of leukemia incidence (10 observed compared with 9.2 expected) among male and female radium dial painters. When analyses were conducted for individuals for whom dosimetry was available, again no excess of leukemia incidence (2 observed compared with 2.04 expected) was observed.

Throughout the studies of US radium dial painters, the excess of bone and head (mastoid) cancers has persisted. A more recent study (Stebbings et al., 1984) of 1285 females employed before 1930 in the US radium dial painting industry examined cancer mortality for sites other than bone and head. When mortality rates among the dial painters were compared with US mortality rates, the SMRs for breast (SMR = 144, 95% CI = 101-199) and colon (SMR = 156, 95% CI = 100-232) cancers were borderline significantly elevated. When the comparison rates were adjusted for regional differences, SMRs for colon and breast cancers were no longer significantly elevated. The SMR for lung cancer, although not statistically significant, remained constantly elevated with and without adjustment for regional rates at 145 and 146, respectively. Three times more multiple myeloma was observed than expected among these dial painters. Because mortality from multiple myeloma was strongly related to duration of employment, the authors (Stebbings et al., 1984) suggested that this excess might be better explained by exposure to external radiation rather than exposure to radium.

A similar investigation (Baverstock et al., 1981) of British luminisers reported an excess of breast cancer among women receiving absorbed doses of at least 20 rads. This excess was statistically significant among women first employed before the age of 30. Although the excess occurred among women working with radium-containing paint, the authors stated that the excess of breast cancer was due to the external radiation exposure received by these women. This assertion was repeated in a follow-up article published in 1983 (Baverstock and Vennart, 1983).

Shipyard Workers

Najarian and Colton (1978) reported greater than a five-fold excess of leukemia (6 observed and 1.1 expected) among nuclear workers employed by the Portsmouth Naval Shipyard. They also reported an observed to expected ratio of 1.78 for all cancers. Expected values were generated using proportional mortality data for US white males.

A subsequent retrospective cohort mortality study of the Portsmouth Naval Shipyard workers reported no excess of leukemia among radiation workers (SMR = 84, 95% CI = 34-174). SMRs for all causes, all cancers and hematopoietic cancers were less than 100. This study, unlike the earlier study, had access to radiation monitoring records, thereby reducing the misclassification of exposure status (Rinsky et al., 1981).

Nuclear Industry Workers

Numerous studies of workers in the nuclear industry have recently been conducted. These studies focus on workers, some of which have been exposed to low levels of radiation over a long period of time. Although exposures were generally low, exceptions do exist and these include persons receiving large exposures in a single event, such as an accident (e.g. a glove box explosion).

Because the nuclear industry generally began in the 1940's with the experimental research programs of the Manhattan Project and the naval nuclear shipyards, sufficient follow-up time for the study of cancer among nuclear workers has only recently elapsed; therefore, many of the investigations of nuclear workers have only recently been published. For example, new studies among workers at the US facilities of Rocky Flats and Hanford, and the British nuclear establishments of the UKAEA (United Kingdom Atomic Energy Authority) and Sellafield, have only recently been released.

Rocky Flats workers. A new study of mortality among employees of the Rocky Flats plutonium weapons facility has been reported recently (Wilkinson et al., 1987). In this report, excess brain tumors were observed among white males employed at least two years. A nonsignificant positive dose-response was observed for brain tumors and external ionizing radiation. This finding is contrary to the results of an earlier case control study of brain tumors among Rocky Flats workers which found no association between brain tumors and radiation exposure, plutonium exposure or job title (Reyes et al., 1984). It should be noted that the case-control study suffered from limited statistical power due to the small number of brain tumor cases (n=16).

Results of the mortality study (Wilkinson et al., 1987) also demonstrated elevated rate ratios for all causes and lymphopoietic cancers when plutonium exposed (>2 nCi) and unexposed (<2 nCi) workers were compared. Rate ratios of 7.69 (90% CI = 0.99, 72.93), 9.86 (90% CI = 1.26, 94.03), and 5.22 (90% CI = 0.57, 38.80) were observed for lymphopoietic cancers at 2, 5, and 10 years induction periods, respectively. Rate ratios for all causes of death were 1.14 (90% CI = 0.91, 1.43), 1.33 (90% CI = 1.05, 1.68), and 1.39 (90% CI = 1.04, 1.87) at 2, 5, and 10 years induction.

Lawrence Livermore workers. Nearly a threefold increase in malignant melanoma was reported among Lawrence Livermore National Laboratory employees compared with expected values based on the population residing near the Livermore Laboratory (Austin et al., 1981). Malignant melanoma was the most common cancer diagnosed among Livermore employees from 1972 through 1977. A later case-control study (Austin and Reynolds, 1984) of melanoma cases diagnosed from 1969 through 1980 reported a relative risk of 3.7 for exposure to radioactive materials. This excess risk remained present when investigators adjusted for other occupational risk factors. No association, however, was found when investigators relied on radiation monitoring badge data (gamma radiation). Nevertheless, researchers concluded that exposure to radioactive materials was the most common occupational risk factor among the cases (65% exposed). They also reported that this exposure, although important, was not sufficient to cause all of the excess of malignant melanoma among these employees. Other occupational risk factors, such as employment as a chemist (RR = 12.9), were also implicated in this study.

Hanford workers. Controversy has surrounded studies of employees at the Hanford Reservation near Richland, Washington. In the most recent report, Gilbert et al. (submitted) continued to observe a correlation between radiation exposure level and multiple myeloma in the Hanford population. This dose response for multiple myeloma had been previously reported (Gilbert and Marks, 1979). Gilbert et al. (submitted) also observed a correlation between radiation dose and female genital cancers. The authors, however, felt that this finding was probably due to chance alone (Gilbert et al., submitted).

Oak Ridge workers. Like Los Alamos and Hanford, the Oak Ridge facility was originally begun in the early 1940's as part of the Manhattan Engineering District. Numerous epidemiologic studies of Oak Ridge workers are under way. Two completed studies are described below.

A mortality study (Polednak and Frome, 1981) of 18,869 white males employed between 1943 and 1947 in a uranium processing plant (Y-12) has been completed. Generally, mortality among the cohort did not differ significantly from the US population. The SMR for lung cancer was borderline significant at 1.09 (95% CI = 0.97, 1.22) but this ratio increased to 1.22 (95% CI = 1.10, 1.36) when a correction was made for underascertainment of death records. Likewise, when corrected for underascertainment, the SMR for leukemia was 1.22 (95% CI = 1.11, 1.35). Both leukemia and lung cancer were among the cancer types hypothesized by the authors to be related to exposure to uranium. SMRs among workers employed in areas suspected to have the highest uranium exposure potential were not remarkable. An elevated SMR for lung cancer among uranium chemistry workers hired at age 45 or older was not adequately explained. Cigarette smoking and exposures to other chemical agents were not considered in these analyses.

Another study of Oak Ridge workers (Checkoway et al., 1985) examined mortality among 8,375 white males employed by the Oak Ridge National Laboratory from 1943 through 1972. SMRs comparing mortality rates for the cohort with expected values based on US mortality rates were calculated. The SMR for mortality from all causes of death was significantly low (SMR = 0.73, $p < 0.01$). SMRs for heart disease (SMR = 0.75), all cancers (SMR = 0.78), lung cancer (SMR = 0.75), digestive diseases (SMR = 0.36), and motor vehicle accidents (SMR = 0.60) were significantly less than expected. SMRs for leukemia (n=6), Hodgkin's disease (n=5), and cancer of the prostate (n=14) nonsignificantly exceeded 1.00 at 1.48, 1.10, and 1.16, respectively. Standardized rate ratios were used to examine dose-response among four "causes" of death, all causes, all cancers, leukemias, and cancers of the prostate. Although nonsignificant, a dose-response was suggested for leukemia at 10 years induction. SRRs were 1.00 for the unexposed, 1.38 for the 0.001-0.999 rem category, and 2.70 for the 1.000-4.999 rem category. No cases were observed among persons receiving $\geq$5 rems of exposure.

<u>British nuclear workers</u>. Beral et al. (1985) reported on mortality among 39,546 persons employed by the United Kingdom Atomic Energy Authority (UKAEA) at one or more of its many establishments. In general, as observed among most workforces, mortality was less than general population rates (in this case rates for England and Wales). SMRs for all causes (SMR = 74), all cancers (SMR = 79), stomach cancer (SMR = 70), lung cancer (SMR = 72), bladder cancer (SMR = 70) and brain cancer (SMR = 60) were significantly less than 100. In addition, SMRs for diseases of the nervous system, circulatory system, respiratory system, digestive system and for deaths from injuries were significantly less than 100. While no cause significantly exceeded 100, six cause-specific cancers demonstrated SMRs equal to or in excess of 100: prostate cancer (SMR = 100, 95% CI = 67, 145), testicular cancer (SMR = 153, 95% CI = 73, 281), thyroid cancer (SMR = 122, 95% CI = 25, 356), all lymphatic and hematopoietic neoplasms (SMR = 102, 95% CI = 80, 128), and the subcategories non-Hodgkin's lymphoma (SMR = 107, 95% CI = 66, 166) and leukemia (SMR = 123, 95% CI = 86, 171). All 10 of the testicular cancers occurred at Harwell resulting in an SMR for testicular cancer of 232 (95% CI = 111, 427) for that facility alone.

When workers were considered on the basis of whether or not they had a radiation record, few differences were observed. Among women, the SMR for uterine/ovarian cancer was 183 for women with a radiation record and 68 for women without a radiation record. When examined by specific cancer site, SMRs for cancers of the uterus were significantly high ($p < 0.05$) among women with a radiation record.

When radiation dose was considered, mortality from cancer of the prostate was found to be significantly related to cumulative radiation exposure. Although not significant, a trend of increasing mortality with increasing radiation dose was observed for leukemia and multiple myeloma. At Harwell and adjacent facilities, the relationship between non-Hodgkin's lymphoma and radiation exposure was significant. Likewise, when the Winfrith facility was considered alone, intestinal cancer was significantly related to radiation exposure level.

Another study of British nuclear workers (Smith and Douglas, 1986) examined mortality among 14,327 workers (1947-1975) employed at the Sellafield plant of British Nuclear Fuels. SMRs for all causes of death were 98 for men (2048 deaths) and 102 for women (229 deaths). For all cancers, the SMRs were 96 and 87 for men and women, respectively. Among radiation workers, no cancer-specific SMRs significantly exceeded 100. SMRs for cancers of the lung, liver, and Hodgkin's disease were significantly less than expected. Although not statistically significant, among radiation workers the SMRs for multiple myeloma and thyroid cancers were 165 and 241, respectively. When dose-response analyses were conducted, a significant negative association was identified for all causes of death and cumulative radiation exposure. A nonsignificant positive dose-response was observed for leukemia and cumulative radiation dose. When a

15-year lag period was employed in the analyses, significant positive dose response relationships with cumulative radiation dose were observed for multiple myelomas, all lymphatic and hematopoietic neoplasms, and bladder cancers. A nonsignficant positive dose response was observed for leukemia.

Los Alamos workers. In 1953, a clinical follow-up study of 29 men thought to have large plutonium body burdens was begun at Los Alamos, under the sponsorship of the Atomic Energy Commission. Eventually, 3 of the subjects were dropped resulting in a group of 26 men believed to be heavily exposed during plutonium operations at Los Alamos during World War II (Hempelmann et al., 1973). The most recently reported results of the clinical studies of Los Alamos workers were published in 1985 (Voelz et al., 1985). This clinical investigation, incorporating 37 years of follow-up, did not reveal any unusual clinical findings for men in this age group. The only cancers observed during the 37 years have been skin cancers among 3 of the subjects. At the time of the 1981-1982 medical examination of the workers only 2 of the 26 workers were deceased, 1 from an accident and the other from a myocardial infarction. Clinical follow-up of these men has continued through the present, with the 22 survivors (2 additional deaths occurred between 1982 and 1986) returning to Los Alamos in 1986-1987 for another round of clinical examinations.

In 1974, the program was expanded to include a cohort mortality study of 241 Los Alamos workers with estimated plutonium body burdens of at least 10 nCi. Of the 241, 224 (92.9%) were white males (Voelz et al., 1978). These individuals have been followed since 1974 with the most recent results reported in 1983 (Voelz et al., 1983). These results indicated a strong healthy worker effect with SMRs for all causes (SMR = 56, 95% CI = 40, 75) and diseases of the circulatory system (SMR = 45, 95% CI = 27, 71) significantly less than expected. The SMR for all cancers was 54 (95% CI = 23, 106) and SMRs for cancers of the lung (SMR = 20, 95% CI = 0, 110) and lymphopoietic cancers (SMR = 67, 95% CI = 1, 370) were quite low. No cancer-specific SMR was significantly elevated.

In approximately 1975, the program was expanded to include epidemiologic studies of plutonium and other radiation workers at six Department of Energy (DOE) contractor facilities: Los Alamos, Rocky Flats, Mound, Hanford, Oak Ridge, and Savannah River. Studies have included ongoing cohort mortality studies and case-control studies of workers at these six facilities. A study of morbidity among plutonium workers is planned and should begin shortly.

Another study (Acquavella et al., 1983a) examined cancer incidence (1969-1978) among Los Alamos employees and reported significantly lower cancer incidence (SIR = 60, 95% CI = 0.46, 0.78) among non-Hispanic white males compared with New Mexico cancer incidence rates. Although no significantly elevated standardized incidence rates (SIRs) were observed, the SIR for lymphosarcoma was suggestively elevated (SIR = 2.49, 95% CI = 0.81, 5.81).

Among non-Hispanic females employed by the Los Alamos National Laboratory (1969-1978), elevated standardized incidence ratios for all cancers, melanoma, cancers of the breast, uterus, eye, thyroid, and brain, other genital cancers, and other lymphatic cancers were observed. For the purpose of generating hypotheses, one-tailed probabilities were calculated and are presented in Table 1. The findings of this study are of special importance because tissues of the breast and thyroid are known to be very radiosensitive, while brain and lymphatic tissues are considered to be less radiosensitive (Committee on the Biological Effects of Ionizing Radiations, 1980).

The investigation of cancer incidence (Acquavella et al., 1983a) had several important limitations. First, the study included only a subset of the population and a very short follow-up period. In addition, the incidence study was restricted to persons employed from 1969 through 1978 (the period covered by the records of the New Mexico Tumor Registry (NMTR)). Cancers included in the study were those diagnosed during employment or during the first six months after termination. Because the incidence study was restricted to a subset of the work force and a limited follow-up period for these subjects, it may not have reflected the true disease rate in the population as a whole. A potential result of these limitations was that cancer cases diagnosed outside New Mexico were missed in the incidence analyses.

The major limitation of the incidence study (Acquavella et al., 1983a) was that exposure data were unavailable and the authors were, therefore, unable to determine whether the observed rates were associated with occupational radiation exposure. The limited follow-up time may not be sufficient to allow for the long latency period required for the development of most tumors. As a result, the tumors diagnosed and included in the incidence study may not have been related to a Laboratory work-place exposure, while health effects related to

TABLE 1

CANCER INCIDENCE AMONG ANGLO FEMALE EMPLOYEES (1969-1978)

Cause* (ICDA-8)***	Observed	Expected	Standardized Incidence Ratio**	P-value** (One-Tailed)
All cancers (140-209)	32	26.44	1.21	0.162
Melanoma (172)	2	1.09	1.83	0.297
Breast cancer (174)	14	9.34	1.50	0.092+
Cervical cancer (180)	1	1.50	0.67	0.558
Uterine cancer (181-182)	2	0.25	8.00	0.026++
Other genital cancers (183-184)	3	1.47	2.04	0.184
Cancer of the eye (190)	1	0.08	12.50	0.077+
Brain cancer (191-192)	2	0.41	4.88	0.064+
Thyroid cancer (193)	3	0.75	4.00	0.040++
Other lymphatic cancer (202,203,208)	2	0.35	5.71	0.049++

*Acquavella, et al. (1983a)

**Rothman and Boice (1979)

***ICDA-8 is the Eighth Revision of the International Classification of Diseases, Adapted for use in the United States

+Significant p = 0.10

++Significant p = 0.05

Laboratory work-place exposures may have gone undetected. Finally, the incidence study was limited by the small number of person-years and observed cases.

Currently, another study of cancer incidence among Laboratory employees is underway. This investigation will incorporate radiation records and will extend follow-up through 1983. Results of this study are anticipated in 1988.

Two studies have examined malignant melanoma among Los Alamos workers, an incidence study (Acquavella et al., 1982) and a case control study (Acquavella et al., 1983b). These studies were conducted in response to the high incidence of malignant melanoma observed among employees of the closely related Lawrence Livermore Laboratory (Austin et al., 1981).

In the melanoma incidence study (Acquavella et al., 1982), no excess incidence of melanoma was observed among white males employed by the Los Alamos National Laboratory (6 cases observed compared with 5.69 expected). In the case-control study, Acquavella et al. (1983b) found no association between melanoma and external radiation exposure, plutonium body burden, or a history of employment as a chemist or as a physicist. Education was, however, positively associated with melanoma.

CHAPTER III

PURPOSE AND SCOPE

A historical cohort study was conducted to examine mortality among 6790 women employed by the Los Alamos Laboratory from 1943-1981. The study addressed two questions. First, it sought to determine whether overall mortality among Los Alamos Laboratory female employees differed significantly from mortality in the US population.

Second, this investigation sought to determine whether cancer mortality among radiation exposed workers differed significantly from nonexposed workers. Exposures to external ionizing radiation and plutonium were considered. These investigations were limited to cancer mortality because experience in populations exposed to low radiation doses indicates that cancer is the primary nongenetic effect expected when an individual is exposed to radiation (United Nations Scientific Committee on the Effects of Atomic Radiation, 1977). In fact, the Committee on the Biological Effects of Ionizing Radiations (1980) "considers cancer induction the most important somatic effect of low-dose ionizing radiation."

There were several reasons that justified conducting the investigation of mortality among Los Alamos female employees. First, there is a need for more investigations of occupational radiation exposure among women. At this time, there have been very few studies of health of women in the workforce and even fewer of women exposed to radiation in their jobs. Since this study was originally proposed, at least two studies have demonstrated health effects in female nuclear industry workers. Gilbert et al. (submitted) has observed a positive relationship between cumulative radiation and all female genital cancers among female Hanford employees. Beral et al. (1985) reported elevated SMRs for genital cancers, especially uterine cancers, among British female radiation workers.

In addition, health effects in radiation exposed women need to be examined because there has been some evidence of a sex difference in physiological responses to radiation exposure. One example of these sex differences was observed in the studies of individuals exposed to x-ray therapy for the treatment of tinea capitis. Exposed women were three times more likely to develop cancer of the thyroid than the treated men (Shore et al., 1976; Ron and Modan, 1980).

Another reason for conducting this study was that the study of cancer incidence among Los Alamos employees (Acquavella et al., 1983a) suggested that women in this cohort may experience elevated rates of some types of radiation-induced cancer. Because of the limitations of this earlier cancer incidence study (Acquavella et al., 1983a), already described, it was important to follow it with a more complete study. The currently reported mortality study of Los Alamos women was more complete because it included all female Laboratory employees hired from 1943-1979 and followed them over a much longer time period. All deaths that occurred in the cohort were considered regardless of the cause, place or date of death (within the study period). As a result, this investigation had more power to detect an effect, if one existed, and was able to take into consideration the important time factors that influence the exposure-disease relationship. A very important advantage of the current mortality investigation was that it considered radiation exposure (external ionizing radiation and plutonium) among members of the cohort and examined the exposure-disease relationship.

CHAPTER IV

METHODS

Acquisition and Computerization of Personnel Data

In 1978, the Health Study of Nuclear Workers acquired microfilmed personnel records for current and former employees of the University of California's Los Alamos Laboratory. Updates for these records, which were obtained in early 1980, were filed with the microfilmed personnel records.

In 1982, trained data analysts employed by the Epidemiology Program began coding and entering the Los Alamos personnel records into a computerized data base (NEW-LA-PEOPLE) according to a detailed coding protocol (Appendix A). The following variables were coded and entered from the personnel records: last name, first name, middle initial(s), title, social security number (SSN), birthdate, birthplace, sex, race, ethnicity, education, z-number (a unique Los Alamos identifier), first job title, date of hire, date of termination, and last or most recent job title. After data entry was completed, each record was randomly assigned a unique study number which insured the confidentiality of study subjects. Due to the difficulties encountered in coding these very long and detailed records, all records were double-entered to improve accuracy. A prompting subroutine in the data entry program signalled the data analyst that the initial entry disagreed with the current entry. The program allowed the analyst to review the initial entry and the personnel record and then enter a corrected entry into the data base.

When the data entry was completed, an extensive review of the data base was conducted. Duplicate records were merged and an effort was made to insure that the resulting record contained the complete information on the individual. The resulting data base contained 23,218 records.

After the review effort, a 10% random sample of the records in the computer data base was selected for an internal consistency check. The purpose of this activity was to assess the accuracy of the computerized data. The 2320 records selected for this check were reedited and errors identified were tabulated. A total of 128 errors were identified, an overall average of 0.78% of the fields or 5.52% of the records displayed errors. Table 2 presents a breakdown of the errors per field (Los Alamos Log, 1983). All but one of the fields contained error rates of $\leq$0.5%. The exception was the field containing education. This variable was difficult to code due to the vast geographical and historical differences in educational systems in this country. On the basis of the results of the internal consistency check, it was judged that the data in the data base were satisfactory for analyses.

When the study of the women in the Los Alamos population was begun, a new data base (LA-FEMALES) containing the subcohort of the women (n=6790) in the population was created. The term "cohort" has

TABLE 2

RESULTS OF AN INTERNAL CONSISTENCY CHECK OF
LOS ALAMOS CODED PERSONNEL DATA

Field	Frequency	Percent
Last Name	2	0.1
First Name	5	0.2
First Middle Initial	4	0.2
Second Middle Initial	1	0.0
Third Middle Initial	0	0.0
Title	4	0.2
Social Security Number	6	0.3
Sex	3	0.1
Race	7	0.3
Education	32	1.4
Birthdate	9	0.4
Birthplace	4	0.2
Hire date	9	0.4
Termination Date	10	0.4
First Job Title	12	0.5
Last Job Title	10	0.4
Z-number	6	0.3
Ethnicity	4	0.2

been used from this point forward to describe these women. The LA-FEMALES data base included the following fields from the overall Los Alamos data base (NEW-LA-PEOPLE) described earlier: study number, last name, title, first name, middle initial(s), SSN, sex, race, ethnicity, education, birthplace, birthdate, hire date, termination date, z-number, first job title, and last or most recent job title.

After existing information was compiled, an effort was undertaken to add additional variables needed for the analyses and to improve the coverage for variables in the data base. For example, at that time race was only identified for 72.0% of the women in the NEW-LA-PEOPLE data base. Fields were added to LA-FEMALES to allow the entry of information on race from a variety of Los Alamos record sources. Information on race and ethnicity was obtained from four different sources of personnel data and from the computerized medical records. The additional data base fields included data on ethnicity from Laboratory personnel records that matched the cohort. These data were then recoded to match the codes used during the coding of race and ethnicity from the personnel records. When this was completed, the information was cross-loaded into the race and ethnicity fields in the data base. For example, race for persons listed as white or Hispanic was coded as white. Numerical codes also had to be recoded to obtain consistency when these records were cross-loaded. A similar process was used for information on race obtained from the Laboratory medical records. A field was added to the LA-FEMALES data base and information on race was loaded into this field from the computerized medical records. This information was then recoded and cross-loaded into the fields race and ethnicity. In no case was the information originally coded from the personnel records overwritten by these additional personnel and medical data sources. The personnel and medical records were only used to supplement the data when the information was missing.

When this process was completed, race had been identified for 97.1% of the cohort (Table 3). The remaining 2.9% of the cohort for whom race was still unknown were considered white for these analyses. This assumption was justified because 97.8% of the cohort (with race known) was white. Furthermore, 1980 US census data (Bureau of the Census, 1982a) indicated that there were 73 (0.4%) Blacks, 99 (0.6%) American Indians, and 191 (1.1%) Asians residing in Los Alamos County in 1980. Of the Blacks, only 32 were females and only 16 were between the ages of 20 and 65 (Bureau of the Census, 1982b). Accordingly, misclassification from this assumption should have been small. In addition, because race was available from most death certificates, race for deceased members of the cohort should have been classified correctly.

Duration of employment was also calculated and entered into LA-FEMALES. A flag indicating whether a person worked at least six months was also entered into the data base.

Additional efforts were undertaken to locate missing birthdates, hire dates, and termination dates from personnel and medical records. When an actual hire or termination date was located, this information was entered into the appropriate field. When evidence was located that an individual was still employed as of a certain date, this information was entered into a new field, DATE-LAST-WORKED (DLW).

TABLE 3

A COMPARISON OF INFORMATION ON RACE IDENTIFIED FROM THE PERSONNEL MICROFICHE AND AFTER EXTENSIVE FOLLOW-UP FROM MANY SOURCES

Race	Personnel Microfiche Frequency	Personnel Microfiche Percent	Complete Follow-up Frequency	Complete Follow-up Percent
White	4815	70.9	6448	95.0
Oriental	16	0.2	28	0.4
American Indian	51	0.8	103	1.5
Black	4	0.1	14	0.2
Unknown/not specified	1904	28.0	197	2.9
Total	6790	100.0	6790	100.0

Only actual termination dates were entered into the termination date field and this was only done when the termination date had been previously unknown. Medical records provided actual termination dates for some persons, but for many individuals the medical records provided evidence that a person was still employed after the end of study. (Definition of the end of study will be discussed later.) Persons having a physical examination after December 31, 1981, were assigned a DLW date of December 31, 1981, indicating they were still actively employed as of that date.

Finally, consistency checks were performed to insure that hire dates preceded termination dates, birthdates preceded both hire and termination dates, and that death dates followed termination dates. All discrepancies were identified and the personnel microfiche were reviewed. Incorrect dates were then corrected based on the results of this review.

Table 4 presents the major personnel variables required for standardized mortality analyses. These variables were more than 90% complete as a result of the efforts undertaken to improve the coverage of variables needed for analyses.

Vital Status Ascertainment and Death Certificate Retrieval and Coding

Vital status ascertainment for this cohort included a number of follow-up methods. First, the cohort was submitted to the Social Security Administration (SSA) for searches of vital status. Rosters of women employed by the Los Alamos Laboratory have been submitted to the

TABLE 4

COMPLETENESS OF MAJOR PERSONNEL VARIABLES

	Frequency	Percent
Study Number	6790	100.0
Sex	6790	100.0
Race	6593	97.1
Birthdate	6781	99.9
Hire Date	6770	99.7
Termination Date*	6780	99.9
Education	6740	99.3

*The end-of-study date, December 31, 1981, was assigned to 1254 persons still actively employed on December 31, 1981. Only 10 individuals had unknown termination dates.

SSA on many occasions, the most recent submissions were in 1982 and twice in 1984. The SSA reviewed its earnings, benefits and death records and identified individuals as "alive", "dead", "unknown" (valid SSN and name, but status unknown), "nonmatched" (name and SSN did not match on SSA records), and "impossible" (SSN was not valid). In each submission a small percentage of individuals were not submitted because of missing or incomplete SSNs. For the two 1984 submissions (SSA842, SSA843), the SSA reviewed its 1982 earnings records; therefore, the "alives" were assumed to be alive on or after January 1, 1982. Therefore, an end-of-study (EOS) date of December 31, 1981 was selected because the "alives" were known to still be alive as of that date. Because the two 1984 SSA submissions (Table 5) served as the primary source of vital status information, the end of study must correspond to this date, December 31, 1981.

The SSA checked the 1980 earnings records for the 1982 submission (SSA82). Because this preceded the end of study of December 31, 1981, this information was only used to establish follow-up through December 31, 1979 for persons for whom later vital status information was not available. Results of the three SSA submissions were matched with the data base and entered into a field corresponding with the appropriate SSA return (SSA82, SSA842, SSA843). A new field, DATE-LAST-ALIVE (DLA), corresponding to the last date an individual was known to be alive was established. For example, individuals denoted as "alive" in either of the 1984 SSA returns (SSA842, SSA843) were assigned a DLA date of December 31, 1981, because they were known to

TABLE 5

RESULTS OF THE TWO 1984 SSA SUBMISSIONS
SSA842 AND SSA843

	SSA842		SSA843	
	Frequency	Percent	Frequency	Percent
Alive	3435	50.6	3735	55.0
Dead	360	5.3	389	5.7
Unknown	2260	33.3	1909	28.1
Nonmatch	286	4.2	271	4.0
Impossible	9	0.1	8	0.1
Not sent	440	6.5	478	7.0
Total	6790	100.0	6790	100.0

still be alive as of that date. This field was used to record DLA for all of the vital status follow-up activities.

In 1985, a roster of the cohort was submitted to the National Death Index (NDI). The NDI matches the rosters it receives against death tapes from all 50 of the United States. At the time this roster was submitted, the NDI was able to match against the death tapes for the years 1979 through 1983. The NDI compared persons submitted with the persons listed on the death tapes on the basis of a number of variables including the last name, first name, SSN, birthdate, state of birth, and father's surname. If a deceased match or matches (based on a predetermined score) was/were identified for a submitted individual, the NDI returned the list of potential matches for each individual. The investigator then determined matches which were reasonable. This required reviewing the personnel records and ordering the death certificates for some of the potential matches to determine which matches were in fact accurate. Only matches determined to be accurate were recorded as deceased in the NDI field in the data base.

The next procedure matched Los Alamos Laboratory records against the LA-FEMALES data base and entered additional vital status information obtained from the personnel records into the data base. New fields were added for each record source checked. Personnel records were checked and individuals who were still actively employed after the EOS date were recorded as "alive" in the corresponding field and their DLA date was entered. Medical records were also reviewed and persons receiving a physical examination after the EOS were denoted as "alive" in the corresponding field and their DLA date was entered.

Persons with vital status remaining unknown after the SSA and NDI submissions and the review of existing Los Alamos Laboratory records, were submitted to the New Mexico Department of Motor Vehicles (DMV). The DMV matched the roster against their records and identified persons with active New Mexico drivers licenses. The DMV provided the person's address, date of last license renewal, and dates of recent citations. Persons were assumed to be alive on the date their drivers license was last renewed or the last date they were issued a citation and these dates were entered into the DLA field. Persons with renewal dates or citations after the EOS were designated as "alive". Addresses for persons last renewing their license prior to the EOS were used in the tracing efforts which will be described next.

Finally, persons with vital status still unknown after the above efforts were completed were traced using telephone and mail techniques. Tracing efforts had to be limited to persons employed at least six months due to severe financial constraints. It was felt that if tracing must be limited due to budgetary concerns, it would be best to omit persons employed for shorter periods of time, because these individuals were less likely to be exposed and would probably contribute little to the investigation.

Tracing former workers provided a challenge because they had to be located, sometimes as much as 40 years after the last known contact. The actual steps used to locate former employees differed for each individual and were influenced by numerous factors such as the length of time passed since termination and the types of information available about the individual.

Los Alamos Laboratory personnel and security records were the initial sources of the information used to locate these former workers. These records contained helpful information which could include 1) current, last known, or forwarding addresses, 2) lists of family members and personal references, 3) schools attended/degrees granted, 4) professional society memberships, 5) religious, social and fraternal organization memberships, 6) home towns, and 7) other valuable clues for locating these individuals.

In general, the search began with the last known addresses and forwarding addresses contained in the personnel and security records. These were especially useful in locating recently terminated employees. When possible, using these addresses, a telephone number was obtained through the telephone operator or through searches of telephone directories in the area.

In this study, many of the subjects' husbands had been employed by the Los Alamos Laboratory. The husband's personnel records were also consulted to provide clues to locating the individual. When located, references and especially relatives could often identify the vital status and location of the former worker. When a relative or reference reported that the study subject was alive, a current address and telephone number was requested. If the study subject was reported to be deceased, a date and place of death was requested. Relatives and references were very helpful in these efforts. Spouses, including those divorced, were also very helpful in locating study subjects.

Another extremely valuable source of information was the college/university attended by the individual. Often the college/university or the alumni association was able to provide the current address for a former student. This was especially true for individuals who had earned a degree at the institution. Some universities were unwilling to release a former student's address due to privacy concerns, but were willing to forward a letter to their former student. Several individuals were located in this manner. Another valuable piece of information that was utilized was the home town of the former employee. This was especially useful for locating employees from small towns. Churches, schools, the post office, newspapers, and other local organizations were contacted. Tribal councils and pueblo governments were also helpful in locating American Indians. These local sources could often help locate a relative or former neighbor who knew the whereabouts of the ex-employee.

Persons for whom an address was located, who could not be reached by telephone, were sent a letter. In some instances, letters requesting information on a former employee were sent to relatives or references.

After all vital status and follow-up activities were completed, information was cross-loaded into a single field, CVS_EOS81, which contained a vital status of "alive", "dead" or "unknown" for all persons as of December 31, 1981. Vital status as of December 31, 1981, was located for 86.9% of the total cohort, 86.9% of the white women, and 93.1% of the white women employed at least six months.

During vital status follow-up, a methodological question arose regarding the adequacy of the NDI for ascertaining vital status.

Deaths identified by the NDI for 1979-1981 were compared with deaths identified by the SSA and tracing for the same period. A total of 130 deaths were identified using all methods for the period 1979-1981. Eighteen (13.8%) deaths not identified by the NDI were identified by the combination of the SSA and tracing.

Of these 18 deaths, all of whom were included in the roster submitted to the NDI, 9 were identified as deceased by the SSA. An additional 9 were identified through tracing. Seven of the 9 identified through tracing had not been submitted to the SSA due to missing or incomplete SSN. The remaining 2 were identified as "unknown vital status" by the SSA. Fifteen (83.3%) of the 18 deaths were confirmed by death certificates. The 3 individuals for whom death certificates could not be obtained had been identified as deceased by the SSA. In the past, the SSA has occasionally reported individuals who were living as deceased. These instances often resulted from persons using a spouse or other relative's SSN. Therefore, at this time it was difficult to say for certain that the 3 unverified deaths were definately deceased. All 18 were white. The majority of these women (10, 55.6%) died in 1979, while 5 (27.8%) died in 1980, and 3 (16.7) died in 1981. This suggests that the NDI may be more efficient for the later years it searches; however, this cannot be conclusively stated. Nine (50.0%) of the women were originally hired during the 1940's, while 3 (16.7%) were hired in the 1950's, 5 (27.8%) were hired in the 1960's and 1 (5.6%) was hired in the 1970's. Only 2 (13.3%) of the deaths confirmed by death certificates were due to cancer. One death was the result of breast cancer (IDCA-8 174X) while the other was due to cancer of the uterus (ICDA-8 182).

Seventeen deaths identified by NDI were not identified by the SSA. These deaths could not be compared with the results of tracing because the tracing was conducted after the NDI results were received. Individuals identified as deceased by the NDI were not traced to determine their vital status. Of the 17 deaths not identified as deceased through SSA follow-up, 5 (29.4%) were not submitted due to missing or incomplete SSNs. Of the remaining 12, 11 (91.7%) were reported as unknown or nonmatched by the SSA, and 1 (8.3%) was reported to be alive. All 17 deaths were white and were verified by death certificates. Three of the 17 (17.6%) died in 1979, 3 (17.6%) died in 1980, and 11 (64.7%) died in 1981. Of those not submitted to the SSA, 1 died in 1980 and 4 died in 1981. When the percentages were adjusted for this, 25% (n=3) died in 1979, 16.7% (n=2) died in 1980, and 58.3% (n=7) died in 1981. This may suggest that the SSA is less reliable in ascertaining deaths closer to the end of the period it reviews. Thirteen (76.5%) of the women were first hired in the 1940's, while 3 (17.6%) were hired in the 1950's, 1 (5.9%) was hired in the 1960's, and none were hired in the 1970's. Similar results were observed among the 18 women not identified as deceased by the NDI. Among these women, 50% were first employed in the 1940's. This probably results from the tendency for workers hired in the 1940's to have been older, and older women were more likely to be deceased. Finally, 6 (35.3%) of these 17 died from cancer. The cause-specific cancers represented were breast cancer (n=2), colon cancer (n=1), lung cancer (n=1), and ill-defined/unspecified cancer (n=2).

The conclusion drawn from this exercise was that a combination of follow-up techniques was required to accurately ascertain deaths in a study population; therefore, EOS for this investigation was not extended to include the period 1982-1983, during which the NDI was the primary source of vital status follow-up.

Once an individual was identified as deceased by one of the above follow-up methods, a death certificate had to be located. When the SSA reported an individual deceased, they provided month and year of death and one of the following: the state of last residence, the state in which the death benefit claim was filed, or the zip code of the funeral director. None of these provided the exact place of death, but they did give a place to begin the search. Death certificates were traced in a similar manner to the vital status tracing. When a date and place of death was obtained, the death certificate was requested from the state department of vital records in the state in which death occurred. Occasionally, certificates were obtained from the city or county health departments. Often, certificates had to be traced a second time because the state or city was unable to locate the certificate. In some instances, the family provided a copy of the certificate when the state health department had repeatedly failed to provide the certificate. Deaths occurring outside the United States provided an additional challenge. These foreign death certificates were requested from the US embassy in the country of death or from the foreign country's consulate in the United States. In this investigation, two deaths occurred outside of the United States. One death certificate was obtained from the American Consulate in Munich, West Germany and the other was obtained from the government of the Canal Zone (Panama).

Deaths identified through tracing had to be obtained in the same fashion. These certificates were first requested from the state or city health department or from the embassy for foreign deaths. Often family members had to be recontacted to provide clarification or additional information. Occasionally, the family had to provide a copy of the death certificate when it could not be located elsewhere.

Deaths identified by the NDI were somewhat different because the NDI provided not only the date and place of death but also the certificate number. Nevertheless, some of these certificates required additional follow-up when the state failed to locate them.

Once death certificates were obtained, they were verified to insure that the certificate was the correct individual. Dates of birth and death, social security number, names, and other available information were checked. Once verified, the date of death and the death certificate's sex and race were entered into the data base. Next, all previous cause of death coding information was deleted from the certificates and these certificates were submitted for cause of death coding by a National Center for Health Statistics trained nosologist hired by the Los Alamos Epidemiology Group. All death certificates were coded to the Eighth Revision of the International Classification of Diseases adapted for use in the United States (ICDA-8) (National Center for Health Statistics, 1968). When death certificates were returned from the nosologist, the ICDA-8 for the underlying cause of death was entered into the data base.

A total of 525 deaths were identified, with 428 deaths occurring on or before December 31, 1981. Of the 428 deaths occurring before the end of study, it was possible to obtain 410 (95.8%) of the death certificates. The 18 death certificates that were not obtained were traced and requested from the vital records departments of the states of death. Unfortunately, these certificates could not be located by the states' vital record departments. Only deaths verified by a death certificate were considered as deceased in the analyses. Deaths for which death certificates were not obtained were treated as lost to follow-up, because it was impossible to confirm the report of death.

Of the 18 women for whom death certificates were not obtained, 16 were white and 2 had race unknown. Five of these women worked less than six months. Fourteen (77.8%) were first hired in the 1940's with the remaining 4 (22.2%) hired in the 1950's. Two (11.1%) were reported to have died in the 1950's, 9 (50%) died in the 1960's, 6 (33.3%) died in the 1970's, and 1 (5.6%) died in 1981. All of these deaths were identified through the SSA. As mentioned earlier, past experience indicated that the SSA has on occasion reported incorrectly that a person was deceased. This might have been the situation with some of the unlocated certificates, although it was impossible to estimate that percentage.

Radiation Exposure Records

Almost from its inception in 1943, some operations at the Los Alamos Laboratory have included work with various types of radiation. The two major forms of radiation exposure include exposure to penetrating ionizing radiation primarily from x-rays and gamma rays and exposure to isotopes of plutonium. Collectively, the penetrating ionizing radiation has been called "external ionizing radiation" because it is capable of penetrating the skin into the body. The plutonium has been referred to as "internal radiation" because it gives off alpha rays that are only capable of traveling short distances and do not normally penetrate the skin. Therefore, plutonium is most hazardous when it is taken into the body via inhalation, ingestion, or a wound.

External Radiation

In 1943, the only technology available for measuring external radiation exposures was the Victoreen pocket ionization chamber which was a personal monitoring device worn by persons working in areas thought to have the potential for exposure to radiation (Hemplemann, 1987; Wiggs, 1987c). These pocket chambers were supplemented with and eventually replaced by film badges for the measurement of external ionizing radiation. When used as personnel monitoring devices, film badges were worn on the body and were used to estimate the radiation absorbed or passing into the body. Complete records for pocket ionization chambers no longer exist. Some pocket chamber data are contained in the individual's personal medical record. Medical records for women employed at any time during the period April 1943 through

February 1945 (a date originally thought to represent the beginning of film badge measurements) were reviewed and any mention of radiation exposure including pocket ionization chamber measurements was abstracted. These data have been used in conjunction with other data to designate radiation workers.

All of the film badge data beginning in 1944 (when film badges were first used) through 1981 have been computerized by the Los Alamos Laboratory Dosimetry Group. The earliest data were "evaluated" to estimate the radiation dose in rems and make it more comparable to later dosimetry data (Littlejohn, 1987; Wiggs, 1987b). The external radiation data are in units known as rem, roentgen equivalent man, which is a "unit of dose equivalent" (Casarett, 1968). This unit is used to convert absorbed dose, measured in rads, into a unit that takes into account the fact that different types of radiation produce different degrees of biological response at the same level of energy deposition in living tissue. Quality factors are used to standardize the dose against the equivalent dose from gamma rays produced by cobalt-60. The rem is a measure used widely for radiation protection activities (Casarett, 1968).

In 1980, the Los Alamos Laboratory switched to the thermoluminescent dosimeter (TLD) to measure external radiation data. These TLDs contain lithium flouride crystals which store energy when exposed to radiation. When heated, these crystals give off light, a measure of which is used to quantify radiation exposure (Casarett, 1968). Like film badges, TLDs are shielded to allow different types of radiations to be measured. These monitors are especially good for measuring exposures to neutrons.

In addition to exposures received at Los Alamos, the computerized dosimetry data included information on previous exposures and exposures received at other facilities and test sites visited by Laboratory employees. These values were included in the lifetime exposures of persons employed by the Los Alamos Laboratory. As with many things, this procedure was not always followed in the earliest days of monitoring, but has been strictly and consistently followed since the 1950's. Also included in the computerized radiation records were the film badge measurements for personnel monitored at the Trinity Test, when the first atomic bomb was detonated (Littlejohn, 1987).

The computerized external radiation data were obtained from the Los Alamos Laboratory's Dosimetry Group and a large effort was undertaken to match these data against the cohort of women employed by the Los Alamos Laboratory. Many problems related to the limited identifying data on the radiation record were encountered. Computerized matches on z-number were made first, followed by name and date matches. All discrepancies or questionable matches were resolved by hand, through review of the personnel records to determine if the individual in the radiation record was the same as in the cohort.

Because the computerized radiation records contained annual exposure summaries, important dates, such as the first sample date, had to be estimated. For example, if an individual was first monitored in the same year she was hired, the first sample date was established as the midpoint between the hire date and the end of the hire year. If an individual was first monitored in her termination year, the first sample date was established as the midpoint between the first day of the termination year and the actual termination date. If the first sample date occurred during a nonhire/nontermination year of the individual's employment, the first sample date was established as the midpoint of the year. Persons with radiation exposures from previous employments were assigned a first sample date equivalent to their hire date. Dates on which an individual attained her first positive sample and cumulative radiation doses of 1, 5, and 10 rem were also calculated. These dates were estimated from the annual exposure records in the same fashion as the first sample date. Persons with previous positive radiation exposures or exposures of at least 1 rem, 5 rems or 10 rems were assigned their hire date for the corresponding dose category. Cumulative radiation dose for an individual from hire date through termination or the EOS, December 31, 1981, was also calculated for monitored study subjects.

Plutonium

In the spring of 1944, the first milligram quantities of plutonium arrived at Los Alamos. Because plutonium was considered to be potentially hazardous, safety regulations were instituted when plutonium chemistry work began at Los Alamos. For example, workers wore coveralls, "booties" (shoe covers), and surgical caps while in the work place. Workers were required to shower and turn in their work coveralls when leaving "D Building", the wooden building in which all plutonium work was originally conducted. Nevertheless, work place exposures to plutonium were inevitable (Hempelmann et al., 1973).

Personal monitoring initially consisted of nose swipes which were counted to reveal alpha activity. In 1944, monitoring was expanded to include a program to collect urine samples after the worker had his/her decontamination shower. By March of 1945, Wright Langham had developed a urine bioassay technique that allowed crude estimates of plutonium body burden (Hempelmann et al., 1973). March of 1945 represented the initiation of the formal urine bioassay program at Los Alamos.

A computer code, PUQFUA, originally developed at Los Alamos in 1959, was used to estimate plutonium body burden from the urine bioassay data (Lawrence, 1978). These plutonium body burdens, which are a measure of plutonium deposited in the body, are calculated at Los Alamos annually using the latest version of the PUQFUA code (III). Data for each urine bioassay for every individual (n >9500) monitored at Los Alamos since 1945 are entered into the PUQFUA III program which calculates a current estimate of plutonium body burden based on the latest excretion model (Wiggs, 1987a).

The 1986 plutonium body burden data were obtained and matched to the cohort. For each individual bioassayed, the following variables were abstracted: first bioassay date, the isotope of plutonium, the number of valid bioassay samples (samples that do not meet the stringent validity checks in the model are considered not valid), last bioassay date for plutonium, the current estimate of nanocurie-years, the nanocurie-years at the last sample, the previous body burden estimate, and the current body burden estimate. Plutonium body burden estimates are measured in nanocuries (nCi), with the current maximum permissible body burden (MPBB) set at 40 nCi (International Commission on Radiation Protection, 1959).

A first positive sample date was hand calculated for each bioassayed study subject. Detailed records containing each bioassay for an individual were reviewed. These detailed records contain a urine activity value in counts or disintegrations per minute (depending on the historical time period). Correction factors for background activity were applied to each measurement for the individual. The correction factors differed across three time periods. Each sample was reviewed and the appropriate correction factor for the date of the sample was subtracted. If the value was still a positive number, this was determined to be a positive uptake. The date of the first positive uptake was recorded for the individual.

For additional details on the history of radiation monitoring at Los Alamos, see Appendix B.

Confounding Exposures

Another difficult problem in analyses such as these is the control of confounding exposures. Operations at Los Alamos have included the potential for exposure to other types of radiation such as polonium-210, uranium-235, and uranium-238. In addition to radioactive exposures, the potential for exposure to chemical hazards has existed. Unfortunately, detailed industrial hygiene records for individuals do not exist prior to the 1970s. Traditionally, monitoring has been done in work areas on an "as needed" basis. Furthermore, because only area monitoring is usually performed, it is difficult, if not impossible, to equate a chemical exposure with an individual. For these reasons, confounding exposures were addressed only in the event of significantly elevated causes of death for which associations with chemicals or radiation exposures have been reported.

Analyses

Development of the Analytic File

An analytic file was created using information from the data base, LA-FEMALES, the medical records, and the plutonium and external radiation records described above. From the LA-FEMALES data base the following variables were obtained: study number, last name, first name, middle initial(s), SSN, z-number, sex, race, education, SSA82 result, CVS_EOS_81 (current vital status as of the EOS date December 31, 1981), ethnicity, first job title, last job title, birthdate, hire date, termination date, date last alive, date last worked, death date, and ICDA-8 code. When all matching activities were completed, the following identifying information was omitted from the file: last name, first name, middle initial(s), SSN, and z-number. The only personal identifier remaining was the unique study number assigned for this study. This technique protected the identity of the study subject and saved valuable space in a very long data record for each individual. The following variables were calculated and added from the external radiation records: first sample date-external, first positive date-external, dates of 1, 5, and 10 rem, and cumulative radiation exposure (dose). An additional flag field, tested-external, was calculated. All persons monitored for external radiation using film or TLD badge, as determined by the first sample date, were flagged as "y". All individuals employed at any time from April 1, 1943 through

February 1, 1945 designated as working or exposed to external radiation exposure in their medical records, were also flagged as "y". All others were assumed to have not worked with external radiation.

The following fields were added from the plutonium exposure data: the isotope of plutonium, number of plutonium bioassay samples, the number of valid plutonium bioassay samples, the first sample date for plutonium, the first positive sample date for plutonium (calculated as described above), the last sample date for plutonium, the nanocurie-years from the last sample, the previous body burden (in nCi), and the current body burden. As with the external radiation flag field, a plutonium flag field was calculated flagging as a "y" all persons with a first bioassay date for plutonium or a mention of plutonium exposure in their medical records (for those persons employed at some time between April 1, 1943 and February 1, 1945). In addition to these flag fields, another radiation flag field was entered into the data base. This field denotes ever-radiation worker ("y") or never-radiation worker ("n"). Persons were designated as radiation workers if any of the following conditions were true: 1) they had a first sample date for external radiation, 2) they had a first sample date for plutonium, or 3) if employed at any time between April 1, 1943 and February 1, 1945, they had any mention of radiation exposure in their Los Alamos Laboratory medical records. Two additional fields were calculated for the analytic file. The first variable, last-term-date, was calculated using the actual termination date and the date last worked. Individuals were assigned the latest of the following: termination date, date-last-worked or EOS date (for persons still employed on or after December 31, 1981). On this basis, only a very few persons (n=10) were assigned an unknown last-term-date. The second variable, duration, was then calculated using the difference between hire date and last-term-date. Only a very few individuals (n=25) had an unknown duration due to a missing hire or last-term-date.

The resulting analytic file contained 6790 records, each containing 38 variables. Table 6 contains a list of the variables.

Descriptive Analysis

The first phase of the analyses consisted of describing the cohort. Frequencies, cross tabulations, and means and medians, where appropriate, were calculated using Biomedical Data Processing Software (BMDP) (BMDP, 1985).

Standardized Mortality Analyses

Overall. The next phase of the analyses consisted of standardized mortality analyses for the cohort. In these analyses, standardized mortality ratios (SMRs) were calculated. The SMR is a measure comparing observed mortality events in the cohort with expected events generated under the assumption that mortality rates for a standard population prevailed in the cohort. The SMR is 100 times the ratio of the observed events divided by the expected events. In these analyses, the MONSON computer program (Monson, 1974) was used to generate sex- and race-specific SMRs which were stratified on age and calendar year (grouped in five-year intervals). The expected values used in these analyses were based on US mortality rates.

TABLE 6

VARIABLES IN THE ANALYTIC FILE

Demograhpic Variables	Radiation Variables
Social security number	Radiation-flag
Sex	Tested-Pu (flag)
Race	Pu isotope
Education	Number of Pu samples
SSA82	Number of valid Pu samples
CVS-EOS-81	First-sample-date-Pu
Ethnicity	First-positive-date-Pu
First job title	Last-sample-date-Pu
Last job title	nCi-years
Birthdate	nCi-last-sample
Hire date	nCi-years-at-last-sample
Term date	Previous Pu body burden (PBB)
Date-last-alive date	Current Pu body burden (CBB)
Date-last-worked date	Tested external (flag)
Calculated duration	First-sample-date-external
Death date	First-positive-date-external
ICDA-8	Date of 1 rem
Death date	Date of 5 rems
ICDA-8	Date of 10 rems
	Calculated cumulative rem
	Calculated-last-term-date

These analyses were limited to all white females employed at any time between April 1, 1943 and January 1, 1979. Nonwhite females were omitted from the analyses because they constituted only a small percentage (2.9%) of the cohort and because the United States mortality rates used for comparison were limited to white females. Including nonwhite females potentially could have biased the results because many mortality rates, especially for cancer, vary between racial groups. For example, in the United States cancer of the cervix is two and a half times more common among black females than among white females. Conversely, white females contract cancer of the uterus twice as often, and cancer of the ovary one and one-half times as often as black females (Young and Pollack, 1982).

Person-years were counted from the hire date, the date on which an individual entered these analyses, until the greatest of the following: death date, termination date (for persons lost to follow-up), 1980 (for persons lost to follow-up but known to be alive in the 1982 SSA return), date last alive, or EOS. For persons with death dates, termination dates, or dates last alive beyond the EOS date, person-years were terminated at EOS date. Deaths were only counted if the individual died in the same period as their follow-up. For example, persons dying after the EOS date were not considered to be deceased in this analysis.

Education. The cohort was stratified on education and SMRs were calculated for women with less than a college degree, women with at least a college degree, and women for whom education was unknown. The category "less than college" included women with little or no education through those who had attended college but had not earned a degree. This category included women with two year associate degrees. The majority of the women in this category were high school graduates. The category of "at least a college degree" included women with bachelor's level degrees and graduate and professional degrees. The unknown education category included women for whom education could not be obtained.

Person years and deaths were counted and SMRs were calculated for the analyses stratified on education in the identical fashion as analyses for all white women. These analyses were also limited to white women, for the same reasons as above.

Duration of employment. Because tracing was limited to persons employed at least six months, vital status follow-up rates differed greatly between those employed six months or more and those employed less than six months. For this reason, standardized mortality analyses were conducted to determine whether differences in mortality existed between persons employed less than six months and those employed six months or more. Persons employed between 1943 and 1979 were included in the analyses. Members of the cohort were dichotomized on the basis of duration of employment (calculated as described above) into two subcohorts. Person-years were calculated from hire date for persons employed less than six months and hire date plus six months for persons employed at least six months to the greater of the following: death date, termination date (for persons lost to follow-up), 1980 (for persons lost to follow-up but known to be alive in the 1982 SSA return), date last alive, or EOS date. For persons with death dates, termination dates, or dates last alive beyond the EOS date, person-years were terminated at EOS date. Deaths were counted only if the individual died in the same period as their person-years were counted.

Persons with unknown durations of employment were automatically omitted from the analyses because they lacked a hire date, a last termination date, or both. Both a hire date and last termination date were required for entry into the MONSON analytic program, and persons with either of these variables missing were automatically omitted from the analyses.

Analyses of Radiation Exposure

Ever/never a radiation worker. The first subcategory includes analyses of "ever a radiation worker" versus "never a radiation worker". Individuals were dichotomized into two subcohorts, "ever radiation worker" and "never radiation worker", on the basis of rad-worker flag described above. Individuals meeting any one of the following conditions were considered "ever radiation worker": 1) they had a first sample date for external radiation, 2) they had a first sample date for plutonium, or 3) if employed at any time between April 1, 1943 and February 1, 1945, they had any mention of radiation exposure in their Los Alamos Laboratory medical records.

These analyses were limited to white females employed at least six months between 1943 and 1979. Because the dates of first radiation exposure were not available for all of these individuals, both subcohorts entered the analyses at their hire date plus six months (0.5 years) to account for the work restriction. If individuals had been allowed to enter the study (that is begin contributing person-years) prior to achieving the six month work restriction, then person time contributed in the interval between hire date and hire date plus six months would be "immortal". That is, because a person was required to work at least six months after hire date and, therefore, live through those six months, no deaths could occur in this interval. Therefore, persons were immortal because they were not at risk of dying in this interval. The only person-years that should be counted in an analyses such as this are person-years-at-risk. "Immortal" person-years are not "person-years-at-risk".

Person-years were counted through the greatest of the following: death date, termination date (for persons lost to follow-up), 1980 (for persons lost to follow-up but known to be alive in the 1982 SSA return), date last alive, or EOS date. For persons with death dates, termination dates or dates last alive beyond the EOS date, person-years were terminated at EOS date. Deaths were only counted if the individual died in the same period as their follow-up.

Because long, although variable, induction times (Rothman, 1986) are required for the development of cancer, a variety of induction periods were employed in these analyses. The shortest reported induction time for exposure to radiation, reported among the "atomic bomb survivors", is two years for the development of leukemia (Committee on the Biological Effects of Ionizing Radiations, 1980). Therefore, induction times of 0 (to serve as a base line), 2, 5, 10, 15, 20, and 25 years were employed in these analyses. The induction periods were additional restriction placed on entry into the cohort.

persons, in all but the 0 years induction analyses, entered the study at hire year plus induction time. For the 0 years induction time, persons entered the study at hire date plus 0.5 years. Both person-years and deaths occurring in the interval between hire date and hire date plus induction time were omitted. Only persons known to be alive at hire date plus induction were allowed to enter the analyses.

The next analyses consisted of directly comparing rates for the "ever-radiation" subcohort and with the "never-radiation" subcohort. Person-years and deaths were calculated as described above for each of the induction times. A sex- and race-specific and age and calendar-year stratified maximum likelihood estimate of the rate ratio was then calculated using a technique described by Rothman and Boice (1979). Ninety-five per cent approximate confidence limits were calculated. For causes of death with cases only in one of the exposure categories, exposed or unexposed, Program 12 of Rothman and Boice (1979) was used to calculate one-sided confidence limits.

An advantage of comparing two subcohorts within the same population was that the impact of the Healthy Worker Effect (HWE) was removed or at least minimized. The Healthy Worker Effect is a type of confounding or selection bias when working populations are compared with the general population. When SMR's are calculated comparing working populations to general populations, the SMR is often below 100. Working populations have been estimated to have mortality rates that are 60-90% of those in the general population. This is due to the fact that working populations must be healthy enough to get and maintain a job, while the general population includes individuals who are too sick to work (McMichael, 1976). Another advantage of comparing within the same cohort was that it controlled for many socioeconomic and regional differences which could not otherwise be controlled.

Ever/never monitored for external radiation. The next analyses were more specific and compared individuals monitored for exposure to external ionizing radiation with those never monitored. The monitored individuals were defined as individuals who wore film badges (1944-1979) or TLDs (1980-1981). No pocket chamber data or qualitative data on radiation exposure were included in these analyses. As with the analyses of "ever radiation" and "never radiation", analyses were limited to white females hired between 1943 and 1979 and employed for at least six months prior to the end of study (December 31, 1981). In addition, persons terminated prior to May 18, 1944 were omitted from the analyses because no film badge monitoring was conducted prior to this date.

Because first sample date for persons monitored for radiation was available, person-years were allocated in a more sophisticated manner. All persons entered the study at hire date plus 0.5 years (to allow for the work restriction). Person-years were counted as "nonmonitored" until the person's first sample date plus appropriate induction period, at which time person-years begin to be counted as "monitored", provided this point in time occurred before the EOS date. Persons who achieved the criteria of first sample date plus induction remained in the study until the greatest of the following: death date, termination date (for persons lost to follow-up), 1980 (for persons lost to follow-up but known to be alive in the 1982 SSA return), date last alive, or EOS date. For persons with death dates, termination dates, or dates last alive beyond the EOS date, person-years were terminated at EOS date. Deaths were only counted if the individual died in the same period as their person-years were counted. If these individuals died after meeting the criteria of first sample date plus induction and before the EOS, their deaths were considered in the "monitored" category. Persons who were never monitored or who achieved the criteria of their "first sample date plus induction" after the EOS, their death date, or the date they were lost to follow-up, remained in the nonmonitored category and only contributed person-years and deaths to that category. These nonmonitored individuals left the study at the greatest of the following: death date, termination date (for persons lost to follow-up), 1980 (for persons lost to follow-up but known to be alive in the 1982 SSA return), date-last-alive, or EOS date. For persons with death dates, termination dates, or dates last alive beyond the EOS date, person-years were terminated at EOS date. Deaths were only counted if the individual died in the same period as their person-years were counted. Deaths occurring among individuals in this category before the EOS were considered as "nonmonitored".

Age and calendar year stratified maximum likelihood estimates of the rate ratio comparing mortality rates for monitored and nonmonitored study subjects and 95% confidence intervals for these rate ratios were calculated in the manner described above (Rothman and Boice, 1979). As in the earlier analyses, induction times of 0, 2, 5, 10, 15, 20, and 25 years were employed in the analyses. Rate ratios were calculated for all causes of death, all malignant neoplasms, and cause-specific causes of cancer for which at least one death was present in each category (monitored and never-monitored).

Comparison of persons with cumulative external radiation exposure greater than or equal to 1 rem compared with those with cumulative exposure less than 1 rem. The next analyses, the most specific examination of external radiation, were limited to persons ever monitored for external radiation between 1944 and 1981. As before, these analyses were also limited to white females hired between 1943 and 1979 and employed at least six months before the EOS. These analyses compared persons with cumulative radiation dose of at least 1 rem with those with less than 1 rem. Persons entered the study at the greatest of first sample date or hire year plus six months (to account for the work restriction). Person-years were counted as "unexposed" until the date an individual achieved 1 rem (plus the appropriate induction period). At this time, the individual began to contribute "exposed" person-years. Exposed persons left the study at death date (if deceased before the EOS), termination date (if lost to follow-up), 1980 (if lost to follow-up but alive in the 1982 SSA return), or EOS. Persons who failed to achieve 1 rem (plus induction) before the death or EOS, left the study at death (if before EOS), termination (if lost to follow-up), 1980 (if lost to follow-up but alive in the 1982 SSA return), or EOS. No individual, exposed or unexposed, contributed person-years or deaths after the EOS.

Among monitored individuals, direct comparisons between persons with at least 1 rem and persons with less than 1 rem were conducted. Maximum likelihood estimates of the rate ratio and 95% confidence limits were calculated as described above. These estimates were sex- and race-specific and adjusted for age and calendar time. Induction times of 0, 2, 5, 10, 15, 20, and 25 years were employed.

Comparison of persons bioassayed for plutonium with those never bioassayed for plutonium. Analyses of potential health effects of plutonium were conducted next. Analyses were limited to persons employed on or after March 1, 1945, the date thought to represent the start of plutonium bioassays. No one entered the study until at least March 1, 1945. The first series of comparisons examined SMRs for persons "ever bioassayed" for plutonium and SMRs for persons "never bioassayed", including person-years for persons eventually monitored until the date of their first bioassay (plus induction). Persons were considered monitored from the date of their bioassay (plus induction) until death (if deceased before the EOS), termination (if lost to follow-up), 1980 (if lost to follow-up but known to be alive in the 1982 SSA return), or EOS. Persons who were not bioassayed before death or EOS, entered the study at hire year plus six months or March 1, 1945, whichever was latest, remained "never monitored" and left the study at death, termination, 1980, or EOS, as described above. When an induction time was employed in the analysis, the person must have achieved their bioassay date plus induction before entering the "monitored" category. As before, no one was allowed to leave the study after the EOS. Induction periods of 0, 2, 5, 10, 15, 20, and 25 years were employed in these analyses.

Maximum likelihood estimates of the rate ratio were calculated to compare rates in the plutonium "monitored" directly with rates for the "nonmonitored". Person-years and deaths in these analyses were allocated in the identical fashion as in the SMR analyses described above.

Comparison of those with ever a positive plutonium uptake with those with never a positive plutonium uptake (bioassayed only). The next series of plutonium analyses were more specific and examined the bioassayed subcohort and calculated SMRs for persons monitored for plutonium with a "positive uptake" and those persons monitored for plutonium with "no positive uptake". Persons entered the study at their first bioassay date or hire year plus six months, whichever was latest. Person-years and deaths occurring up to the first positive sample date plus induction were considered as "no positive uptake", while person-years after the first positive sample date plus induction contributed to the category "positive uptake". Persons left the study at death, termination, 1980, or EOS, as described before. Persons who did not achieve first bioassay date plus induction before death, loss to follow-up, or EOS, only contributed person-years to the "no positive uptake" category. Deaths were counted in an identical fashion as person-years. For example, if an individual died after achieving first positive bioassay date plus induction but before EOS, their death was counted in the category of "positive uptake", or EOS, only contributed person-years to the "no positive uptake". No deaths or person-years were counted after the EOS date. Induction times of 0, 2, 5, 10, 15, 20, and 25 years were calculated.

Survival Analyses

A goal of this study was to describe survival among members of the cohort and to compare survival distributions for the radiation-exposed and unexposed subcohorts. BMDP program P1L was used to calculate survival distributions (BMDP, 1985).

To correspond with the stratified analyses of radiation exposure, survival was calculated for the subcohort of white women employed at least six months. For members of this subcohort, survival time was defined as the time between the first date of hire plus six months and date of death (for deceased before the EOS) or the end-of-study date for censored (alive at EOS) observations. Survival times for observations censored due to loss to follow-up were truncated at date of termination or the last date they were known to be alive. Average survival time was calculated and a plot of the survival distribution calculated by Kaplan-Meier product limit method was generated (BMDP, 1985).

The next analyses considered white women employed at least six months and hired between 1943 and 1979. This subcohort was then divided into two groups, radiation and nonradiation workers, based on the criteria described earlier. Survival times for these mutually exclusive groups were calculated in an identical fashion to the survival times described above. Kaplan-Meier product limit estimates of the survival times for radiation and nonradiation workers were plotted. Average survival times were computed. In addition, two statistics comparing the survival distributions between these two groups were computed. The first statistic was a generalized

Kruskal-Wallis test described by Breslow (Breslow, 1970). The second statistic comparing the distributions was a Mantel-Cox statistic (BMDP, 1985).

Survival among white female employees monitored for external ionizing radiation was compared with survival for white women never monitored for external ionizing radiation. This comparison was limited to women employed at least six months on or after May 18, 1944, the date believed to represent the initiation of monitoring for external ionizing radiation (with film badges). Survival times for these mutually exclusive groups were calculated as described above, except that entry to the analyses was not permitted prior to May 18, 1944. Average survival time, Breslow and Mantel-Cox statistics were calculated. A Kaplan-Meier plot of the survival distributions was generated.

Finally, survival time was calculated for white women monitored for plutonium body burden with bioassay and for white women never monitored for plutonium body burden. These analyses were limited to women employed at least six months. Women had to be employed on or after March 1, 1945, when plutonium bioassays were begun at Los Alamos. Survival times were calculated from hire date plus six months or March 1, 1945, whichever was latest, until death date (if deceased before EOS), EOS date (if alive at EOS), or the date lost to follow-up. Average survival time was calculated and a Kaplan-Meier plot generated. In addition, Breslow and Mantel-Cox statistics were generated.

CHAPTER V

RESULTS

Descriptive Analyses

Race

The cohort included 6790 females ever employed by the Los Alamos Laboratory between 1943 and 1981. Of these 6790 women, 6448 (95.0%) were known to be white. Only 197 (2.9%) persons had race unknown. Because 97.8% of the persons with race known (n=6593) were white, it was decided that persons with unknown race would be considered white in the later analyses. Misclassification resulting from this decision should be small. Among the 410 death certificates obtained for women dying before the end of study, race was identified on 409. Race was identified from personnel sources for the woman whose race was not specified on her death certificate. In addition, a comparison was made between race on the death certificate and in the LA-FEMALES data base. All records in question belonged to women classified as white on one source and as American Indian on the other. Personnel records were searched and proof was located that indicated that all of the records in question (n=7) belonged to American Indians. For example, some of the women were born on Indian Pueblos or attended Indian schools. As a result of these checks, race has been correctly classified for all deceased members of the cohort.

Education

Educational status was another very important characteristic of the cohort (Table 7). The majority of the women (75.5%) in the cohort had no more education than a high school diploma, while 3.4% held associate degrees, 15.9% were college graduates and 4.5% held an advanced degree. The percentages were almost identical for white women, which was not surprising because they comprised the majority of the cohort. Among nonwhite women, the percentages were similar, but reflected a higher level of education. Higher percentages of the nonwhite women finished high school, graduated from college, or possessed an advanced degree, than among the white women.

Employment

Only 20 (0.3%) members of the cohort were missing a valid hire date. For the remaining 6770 (99.7%) of the cohort, the median hire date was 1954.44, approximately May 9, 1944. Table 8 presents the distribution by period of hire. The 1943-1949 period, although only seven years long, was responsible for the largest number of women hired (n=2467, 36.4%). This peak employment was most likely due to the wartime staffing required by the Manhattan Engineering District's Project Y operations at Los Alamos. While white women closely resembled the total cohort, nonwhite women displayed a very different pattern of hire dates. Over half (52.4%) of the nonwhite women in the cohort were originally hired in 1970 or later. This compares to only 22.9% of the white women who were originally hired in 1970 or later.

TABLE 7

EDUCATION FOR THE COHORT OF LOS ALAMOS

Education	All Women		White Women		Nonwhite Women	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
Less than high school	1402	20.7	1377	20.7	25	17.2
High school graduate	3725	54.9	3641	54.8	84	57.9
Associate degree	232	3.4	227	3.4	5	3.5
College graduate	1078	15.9	1054	15.9	24	16.6
Post graduate degree	303	4.5	296	4.5	7	4.8
Unknown	50	0.7	50	0.8	0	0.0
Total	6790	100.0	6645	100.0	145	100.0

TABLE 8

HIRE DATES BY PERIOD FOR LOS ALAMOS WOMEN

Period of Hire	All Women		White Women		Nonwhite Women	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
1943-1944	655	9.7	642	9.7	13	9.0
1945-1949	1812	26.8	1794	27.1	18	12.4
1950-1954	1000	14.8	985	14.9	15	10.3
1955-1959	647	9.6	637	9.6	10	6.9
1960-1964	505	7.5	500	7.6	5	3.5
1965-1969	561	8.3	553	8.3	8	5.5
1970-1974	677	10.0	641	9.7	36	24.8
1975-1979	897	13.2	857	12.9	40	27.6
1980-1981	16	0.2	16	0.2	0	0.0
Total	6770	100.0	6625	100.0	145	100.0

When missing termination dates (n=10, 0.1%) and termination dates for employees active at the EOS (n=1254, 18.5%) were omitted, the median termination date was 56.34 or approximately May 4, 1956.

A more meaningful indication of employment periods of these women was obtained by examining the last-termination-date (Table 9). This variable included valid termination dates for terminated employees and assigned the EOS date (December 31, 1981) for persons actively employed at the EOS (n=1254, 18.5%). Persons who were not active at the EOS whose true termination date was unknown (n=10, 0.1%) were treated as missing values. The median last-termination-date was 62.53 or approximately July 12, 1962. The large number of terminations in the period 1980 and later is due to the assignment of December 31, 1981, to employees active at the EOS. When this period was disregarded, the 1945-1949 period represented the highest percentage of terminations for the cohort and for the subcohort of white women. This was due to the large number of persons terminating at the end of World War II, when the future of the Los Alamos Laboratory appeared uncertain. The nonwhite women did not show the same pattern of termination because, as described earlier, the majority of the women were hired in 1970 or later. Therefore, the majority of terminations in nonwhite women must have occurred in 1970 or later.

Duration of employment was calculated for all members of the cohort. Duration of employment consisted of the difference between hire date and termination date (or active date for persons still employed on December 31, 1981). Only 25 persons had unknown durations

TABLE 9

LAST-TERMINATION-DATE BY PERIOD BY RACE
FOR LOS ALAMOS WOMEN

Time Period	All Women		White Women		NonWhite Women	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
1943-1944	301	4.4	297	4.5	4	2.8
1945-1949	1448	21.4	1441	21.7	7	4.8
1950-1954	849	12.5	830	12.5	19	13.1
1955-1959	570	8.4	557	8.4	13	9.0
1960-1964	440	6.5	433	6.5	7	4.8
1965-1969	527	7.8	524	7.9	3	2.1
1970-1974	465	6.9	442	6.7	23	15.9
1975-1979	597	8.8	574	8.7	23	15.9
1980-1981	1583	23.3	1537	23.2	46	31.7
Total	6780	100.0	6635	100.0	145	100.0

of employment. The distribution of duration was highly skewed with a mean duration of 5.74 years and a median duration of 2.26 years. Over 81% were employed less than 10 years. The longest duration of employment recorded was 38.75 years. All of the nonwhites employed at least 20 years were American Indians. Table 10 presents a breakdown of the cohort by duration of employment.

Vital Status

Vital status (Table 11) as of December 31, 1981, was identified for 86.9% of the cohort. Because tracing efforts were limited to white females who were employed at least six months, the proportion of this subcohort with known vital status was much higher (93.1%).

Radiation Exposure

A total of 1714 (25.2%) women were identified as ever being a radiation worker by the process described in the Methods Chapter. Of these 1714, 1683 (98.2%) were white. When the percentages of radiation workers and nonradiation workers hiring per time period were compared (Table 12), a steadily increasing proportion of the women hiring became radiation workers. Only 12.5% of the women hired in 1943-1945 became radiation workers compared with 40.4% in the period 1975-1979. Twenty women with unknown hire dates were omitted, as were 16 women first hired after December 31, 1979.

There were 1519 women monitored for exposure to external radiation betweeen 1945 and 1981 using either a film badge or a TLD (beginning in 1980). Only 29 (1.9%) of those monitored were nonwhite.

TABLE 10

DURATION OF EMPLOYMENT BY RACE FOR LOS ALAMOS WOMEN

Duration	All Women		White Women		NonWhite Women	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
< 1.00 year	2162	32.0	2114	31.9	48	33.1
1.00- 4.99 years	2269	33.5	2227	33.6	42	29.0
5.00- 9.99 years	1102	16.3	1066	16.1	36	24.8
10.00-14.99 years	396	5.9	385	5.8	11	7.6
15.00-19.99 years	295	4.4	294	4.4	1	0.7
20.00-24.99 years	211	3.1	211	3.2	0	0.0
25.00-29.99 years	182	2.7	180	2.7	2	1.4
30.00-34.99 years	111	1.6	108	1.6	3	2.1
35.00-39.99 years	37	0.5	35	0.5	2	1.4
Total	6765	100.0	6620	99.8	145	100.0

TABLE 11

VITAL STATUS AS OF DECEMBER 31, 1981 FOR FEMALES EMPLOYED BY THE LOS ALAMOS NATIONAL LABORATORY FROM 1943 THROUGH 1981

	Everyone		White Females		White Females Employed at Least 6 mos	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
Alive	5468	80.5	5349	80.5	4558	86.6
Dead	430	6.3	426	6.4	342	6.5
Unknown	892	13.1	870	13.13	361	6.9
Total	6790	100.0	6645	100.0	5261	100.0

TABLE 12

HIRE DATES* FOR RADIATION/NONRADIATION WORKERS: 1943-1979**

Time Period	Radiation Workers		Nonradiation Workers		Total	
	Frequency	Percent	Frequency	Percent	Frequency	Percent
1943-1944	82	12.5	573	87.5	655	100.0
1945-1949	273	15.1	1539	84.9	1812	100.0
1950-1954	241	24.1	759	75.9	1000	100.0
1955-1959	197	30.4	450	69.6	647	100.0
1960-1964	158	31.3	347	68.7	505	100.0
1965-1969	170	30.3	391	69.7	561	100.0
1970-1974	227	33.5	450	66.5	677	100.0
1975-1979	362	40.4	535	59.6	897	100.0

*20 cases had missing hire dates and were omitted.
**16 cases hired after December 31, 1979 were omitted.

Table 13 presents the distribution by first monitoring date for women ever monitored for external radiation and demonstrates a clear increase in frequency for the period 1975-1979. Because the 1980-1981 category contains data for only two years, it is difficult to assess the true frequency for the post 1979 period.

Only 538 (7.9%) members of the cohort were bioassayed for plutonium exposure. Only 10 (1.9%) of the bioassayed group were nonwhite. The frequency distribution of first bioassay dates (Table 14) reveals peaks in the 1945-1949 (20.8%) and the 1975-1979 (28.3%) periods.

STANDARDIZED MORTALITY ANALYSES

Overall SMRs

Standardized mortality ratios (SMRs) were generated for all of the white females in the cohort. As explained earlier, persons with race "unknown" were considered white in the analyses. Only four deaths occurred among nonwhites in the cohort. All four deaths were American Indians, two died of alcoholic cirrhosis of the liver (ICDA-8 5710), one died of sclerosis (ICDA-8 7340) and one died in an automobile collision (ICDA-8 8120).

Standardized mortality analyses were limited to persons hired between 1943 and 1979. A review of the records showed only 40 eligible cohort members hired between January 1, 1979 and December 31, 1981. This poor coverage of persons hired after the first of 1979 was obviously due to incomplete microfilming of personnel record updates.

TABLE 13

DISTRIBUTION OF FIRST MONITORING DATE FOR WOMEN EVER MONITORED FOR EXPOSURE TO EXTERNAL RADIATION

Period of First Monitoring	Frequency	Percent
1943-1944	0	0.0
1945-1949	81	5.3
1950-1954	181	11.9
1955-1959	192	12.6
1960-1964	170	11.2
1965-1969	158	10.4
1970-1974	151	9.9
1975-1979	474	31.2
1980-1981	112	7.4
Total	1519	100.0

TABLE 14

DISTRIBUTION OF FIRST PLUTONIUM BIOASSAY DATE
FOR WOMEN IN THE LOS ALAMOS COHORT

Time Period of First Plutonium Bioassay	Frequency	Percent
1943-1944	0	0.0
1945-1949	110	20.4
1950-1954	63	11.7
1955-1959	53	9.9
1960-1964	35	6.5
1965-1969	34	6.3
1970-1974	41	7.6
1975-1979	152	28.3
1980-1981	50	9.3
Total	538	100.0

These 40 individuals only contributed 78.3 (0.06%) out of 132749.1 person-years and no deaths. It was decided that it would be preferable to include only years for which the ascertainment of employment records was more complete.

Another group of 32 individuals, omitted from the analyses, were women missing a hire date, termination date, or birthdate, because the Monson Program requires this information to calculate SMRs.

The remaining cohort included 6573 persons or 98.9 of the white females in the original cohort. The EOS date was December 31, 1981 for these analyses. Characteristics of the cohort are presented in Table 15.

Standardized mortality ratios for the cohort are presented in Table 16. In most cases, SMRs indicated mortality less than expected based on US death rates. In no case was mortality significantly more than expected. SMRs exceeding 100 included cancers of the skin, uterus, kidney, mental disorders, respiratory illnesses, senility and ill-defined conditions, all injuries, all accidents, motor vehicle accidents and suicides. Ninety-five percent confidence intervals included 100 for each of these causes. Mortality was significantly low for many causes of death, including all causes, all cancers, cancers of the digestive system, cervix, and diseases of the circulatory system. Mortality was only 76% of that expected, based on US death rates. The remaining causes of death were less than expected, although their 95% confidence intervals included 100. No cases of cancers of the larynx, bone, eye or thyroid were observed.

TABLE 15

CHARACTERISTICS OF THE WHITE FEMALES EMPLOYED BETWEEN 1943 AND 1979

Total persons	6573
Total person-years	132670.8
Total number deceased	403
Average age of entry	27.80
Average year of entry	1957.69
Average age of death	57.21
Average year of death	1972.23
Average length of follow-up (years)	20.18
Crude mortality rate (per 100,000 person-years)	303.76

TABLE 16

STANDARDIZED MORTALITY RATIOS FOR 6573 WHITE FEMALES
EMPLOYED BY THE LOS ALAMOS NATIONAL LABORATORY
FROM 1943 TO 1979

Cause (ICD)	Observed	Expected	SMR	95% CI
All causes (001-998)	403	530.33	76	69, 84
All cancers (140-209)	133	171.11	78	65, 92
Oral cancer (140-149)	2	2.40	83	9, 301
All digestive (150-159)	17	36.47	47	27, 75
Esophagus (150)	1	1.32	76	1, 422
Stomach (151)	1	4.64	22	0, 120
Large intestine (153)	9	15.98	56	26, 107
Rectum (154)	2	3.75	53	6, 193
Liver and gallbladder (155-156)	1	3.21	31	0, 173
Pancreas (157)	3	6.48	46	9, 135
All respiratory (160-163)	19	20.99	91	54, 141
Larynx (161)	0	0.52	0	0, 704
Lung (162)	19	20.12	94	57, 148
Bone (170)	0	0.67	0	0, 547
Skin (172,173)	5	2.71	185	60, 431
Breast (174)	36	42.31	85	60, 118
All genital organs (180-184)	20	29.63	68	41, 104
Cervix uteri (180)	2	9.56	21	2, 76
Corpus uteri (181-182)	6	5.33	113	41, 245
All uterus (180-182)	8	15.63	51	22, 101
Other genital organs (183-184)	12	13.89	86	45, 151
Bladder (188)	1	1.47	68	1, 378
Kidney (189)	6	2.44	246	90, 536
Eye (190)	0	0.15	0	0,2389
Brain/CNS (191-192)	5	5.25	95	31, 222
Thyroid (193)	0	0.52	0	0, 701
All lymphopoietic (200-209)	10	14.53	69	33, 127
Lymphosarcoma (200)	2	3.17	63	7, 228
Hodgkins (201)	1	1.89	53	1, 294
Leukemia (204-207)	4	5.65	71	19, 181
Other lymphatic (202,203,208)	3	3.63	83	17, 241
Benign (210-239)	2	3.24	62	7, 223
Mental disorders (290-317)	5	2.44	205	66, 479
All circulatory (390-458)	130	197.27	66	55, 78
All respiratory (460-519)	28	23.35	120	80, 173
All digestive (520-577)	23	29.54	78	49, 117
All genito-urinary (580-629)	5	9.09	55	18, 128
Senility and ill defined (780-799)	6	5.89	102	37, 222
All injuries (E800-998)	51	44.92	114	85, 149
All accidents (E800-949)	32	27.81	115	79, 162
Motor vehicle accidents (E810-827)	18	15.26	118	70, 186
Suicide (E950-959)	14	12.55	112	61, 187
Cancer residual	12	11.57	104	

Education

The cohort was divided into three educational categories, persons with less than a college degree, persons with at least a college degree, and persons with unknown education. Out of the 6573 white females eligible for MONSON, 5196 had less than a college degree, 1338 had at least a college degree, and 39 had education unknown. Table 17 gives the breakdown of the persons, person-years, and deaths by educational category.

Table 18 presents a standardized mortality ratios for the 5196 women who did not have a college degree or a graduate degree. This group includes a range of education including women with almost no education through women who attended college but did not graduate. Women with associate degrees are included in this group.

No cause of death was significantly elevated among this group. SMRs for all causes, all cancers, cancers of the digestive tract, cancers of the colon, cancers of the cervix, and circulatory diseases were significantly less than 100.

Table 19 presents SMRs for white women with at least a college education. To be included in this group, women had to have at least a college degree and some possessed advanced degrees. Among college educated women the SMR for cancer of the kidney (SMR = 646, 95% CI = 130, 1889) and the SMR for mental disorders (SMR = 629, 95% CI = 126, 1838) were significantly elevated. The SMR for all circulatory diseases (SMR = 55, 95% CI = 33, 85) was significantly less than 100. Ninety-five percent confidence intervals for the remaining SMRs included 100.

TABLE 17

CHARACTERISTICS OF THE WHITE FEMALES
BY EDUCATIONAL STATUS

	Everyone	Less than College Graduate	At least College Graduate	Education Unknown
Persons	6573	5196	1338	39
Person-years	132670.8	106029.3	26019.1	622.2
Deaths	403	315	85	3
Cancer deaths	133	98	33	2
Average age of entry	27.80	27.33	29.32	38.17
Average year or entry	1957.69	1957.27	1959.27	1958.91
Average age of death	57.21	57.87	54.34	69.51
Average year of death	1972.23	1972.46	1971.38	1971.50
Average length of follow-up (years)	20.18	20.41	19.45	15.95
Crude mortality rate (per 100,000 person-years)	303.76	297.09	326.68	482.16

TABLE 18

STANDARDIZED MORTALITY RATIOS FOR WHITE FEMALES
EMPLOYED BY THE LOS ALAMOS NATIONAL LABORATORY
FROM 1943 THROUGH 1979 WITH EDUCATION
LESS THAN COLLEGE DEGREE

Cause	Observed	Expected	SMR	95% CI
All causes	315	425.09	74	66, 83
All cancers	98	136.38	72	58, 88
Oral cancer	2	1.91	105	12, 378
All digestive	12	29.22	41	21, 72
Esophagus	1	1.05	95	1, 529
Stomach	1	3.72	27	0, 149
Large intestine	5	12.80	39	13, 91
Rectum	2	3.00	67	7, 240
Liver and gallbladder	1	2.58	39	1, 216
Pancreas	2	5.19	39	4, 139
All respiratory	16	16.66	96	55, 156
Lung	16	15.97	100	57, 163
Bone	0	0.54	0	0, 679
Skin	3	2.15	139	28, 407
Breast	24	33.62	71	46, 106
All genital organs	16	23.59	68	39, 110
Cervix uteri	1	7.60	13	0, 73
Corpus uteri	5	4.27	117	38, 273
All uterus	6	12.45	48	18, 105
Other genital organs	10	11.06	90	43, 166
Bladder	1	1.18	84	1, 470
Kidney	3	1.95	154	31, 450
Eye	0	0.12	0	0,2982
Brain/CNS	5	4.17	120	39, 280
Thyroid	0	0.42	0	0, 873
All lymphopoietic	8	11.62	69	30, 136
Lymphosarcoma	2	2.53	79	9, 285
Hodgkins	1	1.51	66	1, 368
Leukemia	3	4.52	66	13, 194
Other lymphatic	2	2.90	69	8, 249
Benign	2	2.58	78	9, 280
Mental disorders	2	1.94	103	12, 373
All circulatory	110	159.21	69	57, 83
All respiratory	24	18.70	128	82, 191
All digestive	19	23.53	81	49, 126
All genito-urinary	3	7.28	41	8, 120
Senility and ill defined	6	4.70	85	23, 218
All injuries	37	35.93	103	72, 142
All accidents	23	22.33	103	65, 155
Motor vehicle accidents	11	12.29	89	45, 160
Suicide	10	9.97	100	48, 185
Cancer residual	8	9.23	87	

TABLE 19

STANDARDIZED MORTALITY RATIOS FOR WHITE FEMALES EMPLOYED BY THE LOS ALAMOS NATIONAL LABORATORY FROM 1943 THROUGH 1979 WITH AT LEAST A COLLEGE DEGREE

Cause (ICD)	Observed	Expected	SMR	95% CI
All causes	85	98.77	86	69, 106
All cancers	33	33.05	100	69, 140
Oral cancer	0	0.47	0	0, 784
All digestive	5	6.80	74	24, 172
Esophagus	0	0.25	0	0, 1460
Stomach	0	0.86	0	0, 427
Large intestine	4	2.99	134	36, 343
Rectum	0	0.70	0	0, 524
Liver and gallbladder	0	0.59	0	0, 622
Pancreas	1	1.21	83	1, 459
All respiratory	2	4.14	48	5, 174
Lung	2	3.97	50	6, 182
Bone	0	0.12	0	0, 2941
Skin	2	0.53	375	42, 1352
Breast	12	8.34	144	74, 251
All genital organs	4	5.76	69	19, 178
Cervix uteri	1	1.89	53	1, 295
Corpus uteri	1	1.00	100	1, 555
All uterus	2	3.04	66	7, 238
Other genital organs	2	2.71	74	8, 267
Bladder	0	0.26	0	0, 1389
Kidney	3	0.46	646	130, 1889
Eye	0	0.03	0	0, 12736
Brain/CNS	0	1.03	0	0, 355
Thyroid	0	0.10	0	0, 3793
All lymphopoietic	1	2.77	36	0, 201
Lymphosarcoma	0	0.61	0	0, 605
Hodgkins	0	0.37	0	0, 997
Leukemia	1	1.08	93	1, 517
Other lymphatic	0	0.69	0	0, 533
Benign	0	0.63	0	0, 579
Mental disorders	3	0.48	629	126, 1838
All circulatory	19	34.74	55	33, 85
All respiratory	4	4.35	92	25, 235
All digestive	4	5.74	70	19, 178
All genito-urinary	2	1.70	117	13, 424
Senility and ill defined	2	1.13	177	20, 639
All injuries	14	8.71	161	88, 270
All accidents	9	5.29	170	78, 323
Motor vehicle accidents	7	2.89	242	97, 499
Suicide	4	2.52	159	43, 406
Cancer residual	4	2.22	180	

Table 20 presents SMRs for the 39 individuals for whom education could not be determined from the personnel records. Only three deaths were observed among this group. Two of these deaths were due to cancer. A lung cancer (SMR = 584, 95% CI = 8, 3249) and a multiple myeloma (SMR = 2413, 95% CI = 32, 13423) were observed. The noncancer death, which was due to circulatory disease (arteriosclerotic heart disease), had an SMR of 30 (95% CI = 0, 168).

SMRs by Duration of Employment

The next standardized mortality analyses examined the question of duration of employment. Because tracing had to be limited to persons employed at least six months due to financial constraints, follow-up was, therefore, much more limited among those employed less than six months. For this reason, it was decided to limit the remainder of the analyses to persons employed at least six months.

In order to better understand the characteristics of persons employed less than six months, an SMR analysis of these individuals was conducted. This analysis included white females first employed between 1943 and 1979 who had worked less than six months before the EOS. As with the earlier MONSON run, persons with missing hire dates, termination dates, or birthdates were excluded from the analyses. Therefore, persons with missing durations of employment were automatically excluded from the analyses. There were 1339 persons meeting these criteria who were employed less than six months. Seventy-six of these individuals were deceased. Table 21 presents the characteristics of the persons employed less than six months.

TABLE 20

STANDARDIZED MORTALITY RATIOS FOR WHITE FEMALES EMPLOYED BY THE LOS ALAMOS NATIONAL LABORATORY FROM 1943 THROUGH 1979 WITH EDUCATIONAL ATTAINMENT UNKNOWN

Cause (ICD)	Observed	Expected	SMR	95% CI
All causes	3	6.47	46	9, 135
All cancers	2	1.68	119	13, 430
Lung	1	0.17	584	8, 3249
Other lymphatic cancers	1	0.04	2413	32,13423
All circulatory	1	3.32	30	0, 168

TABLE 21

CHARACTERISTICS OF THE WHITE FEMALES
EMPLOYED LESS THAN SIX MONTHS

Total persons	1339
Total person-years	23369.2
Total number deceased	76
Average age of entry	26.15
Average year of entry	1953.47
Average age of death	59.16
Average year of death	1970.60
Average length of follow-up (years)	17.45
Crude mortality rate (per 100,000 person-years)	325.21

Standardized mortality ratios for individuals employed less than six months are presented in Table 22. As with the overall cohort, significant deficits of mortality from all causes, all malignant neoplasms, and all circulatory diseases were observed. None of the SMRs were significantly elevated. SMRs greater than 100 were observed for lung cancer (SMR = 134, 95% CI = 43, 313), kidney cancer (SMR = 213, 95% CI = 3, 1187), brain cancer (SMR = 104, 945% CI = 1, 576), lymphosarcoma (SMR = 165, 95% CI = 2, 920), and lymphatic cancers (SMR = 144, 95% CI = 2, 800). These standardized mortality ratios were based on few cases and their confidence intervals were wide. As with the overall cohort, deaths from injuries were nonsignificantly elevated with an overall injury SMR of 126 (95% CI = 60, 231), an SMR of 148 (95% CI = 30, 380) for motor vehicle accidents, and an SMR for suicide of 139 (95% CI = 28, 407).

When standardized mortality ratios were calculated for persons employed at least six months, person-years were not counted until hire date plus six months to account for the six month work restriction. If person-years had been counted in the interval between hire date and hire date plus six months, these person-years would have been immortal. Future standardized mortality ratios and rate ratio analyses will employ the work restriction and, therefore, this analyses defines the cohort for the future analyses considering exposure. Table 23 presents the characteristics of this subcohort.

TABLE 22

STANDARDIZED MORTALITY RATIOS FOR 1339 WHITE FEMALES EMPLOYED LESS THAN SIX MONTHS

Cause (ICD)	Observed	Expected	SMR	95% CI
All causes	76	104.83	73	57, 91
All cancers	21	32.62	64	40, 98
Oral cancer	0	0.46	0	0, 794
All digestive	2	7.24	28	3, 100
Esophagus	0	0.26	0	0, 1412
Stomach	0	0.93	0	0, 394
Large intestine	0	3.15	0	0, 116
Rectum	1	0.75	133	2, 741
Liver and gallbladder	0	0.65	0	0, 568
Pancreas	1	1.28	78	1, 436
All respiratory	5	3.90	128	41, 299
Larynx	0	0.10	0	0, 3680
Lung	5	3.73	134	43, 313
Bone	0	0.13	0	0, 2813
Skin	0	0.49	0	0, 753
Breast	3	7.88	38	8, 111
All genital organs	3	5.68	53	11, 154
Cervix uteri	0	1.78	0	0, 206
Corpus uteri	1	1.05	95	1, 530
All uterus	1	3.03	33	0, 184
Other genital organs	2	2.63	76	9, 275
Bladder	0	0.30	0	0, 1212
Kidney	1	0.47	213	3, 1187
Eye	0	0.03	0	0,12285
Brain/CNS	1	0.97	104	1, 576
Thyroid	0	0.10	0	0, 3572
All lymphopoietic	2	2.75	73	8, 263
Lymphosarcoma	1	0.60	165	2, 920
Hodgkins	0	0.35	0	0, 1061
Leukemia	0	1.07	0	0, 343
Other lymphatic	1	0.70	144	2, 800
Benign	0	0.63	0	0, 585
Mental disorders	0	0.45	0	0, 820
All circulatory	26	41.32	63	41, 92
All respiratory	6	4.65	129	47, 281
All digestive	6	5.62	107	39, 232
All genito-urinary	1	1.84	54	1, 302
Senility and ill defined	0	1.09	0	0, 338
All injuries	10	7.96	126	60, 231
All accidents	5	5.05	99	32, 231
Motor vehicle accidents	4	2.70	148	40, 380
Suicide	3	2.16	139	28, 407
Cancer residual	4	2.22	180	

TABLE 23

CHARACTERISTICS OF THE WHITE FEMALES
EMPLOYED AT LEAST SIX MONTHS

Total persons	5234
Total person-years	106684.3
Total number deceased	327
Average age of entry	28.72
Average year of entry	1959.27
Average age of death	56.76
Average year of death	1972.6
Average length of follow-up (years)	20.38
Crude mortality rate (per 100,000 person-years)	306.51

Table 24 presents standardized mortality ratios for the subcohort of white females employed at least six months. Significant deficits in mortality were observed for all causes (SMR = 77, 95% CI = 69, 86), all cancers (SMR = 81, 95% CI = 67, 98), digestive cancers (SMR = 52, 95% CI = 29, 85), cancers of the cervix (SMR = 26, 95% CI = 3, 94), and diseases of the circulatory system. No significantly elevated SMRs were observed. Of the standardized mortality ratios elevated over 100, cancers of the skin (SMR = 227, 95% CI = 73, 530), and cancers of the kidney (SMR = 255, 95% CI = 82, 595), and mental illnesses (SMR = 253, 95% CI = 82, 591) stood out. The 95% intervals for these standardized mortality ratios all included 100. Elevated standardized mortality ratios for injuries and cause-specific types of injury death were also observed.

Analyses of Radiation Exposure

Radiation Workers Compared with Nonradiation Workers

Workers were characterized as "ever radiation worker" or "never radiation worker" on the basis of the external radiation monitoring records, the plutonium bioassay records, and the medical records. Analyses included all white females first employed between April 1, 1943 and December 31, 1978. These females had to have been employed at least six months prior to the EOS date of December 31, 1981. Persons entered the study at hire year plus six months (or induction period when that exceeded six months) and remained in the same exposure category throughout these analyses. Persons left the analyses at the greater of death date, termination, or 1980 (if lost to follow-up), or EOS (if alive at end of study). No person-years or deaths were

TABLE 24

STANDARDIZED MORTALITY RATIOS FOR WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS

Cause (ICD)	Observed	Expected	SMR	95% CI
All causes	327	422.02	77	69, 86
All cancers	112	137.69	81	67, 98
Oral cancer	2	1.93	103	12, 374
All digestive	15	29.10	52	29, 85
Esophagus	1	1.06	95	1, 527
Stomach	1	3.68	27	0, 151
Large intestine	9	12.77	70	32, 134
Rectum	1	2.98	34	0, 187
Liver and gallbladder	1	2.55	39	1, 218
Pancreas	2	5.19	39	4, 139
All respiratory	14	17.04	82	45, 138
Larynx	0	0.42	0	0, 872
Lung	14	16.34	86	47, 144
Bone	0	0.53	0	0, 693
Skin	5	2.20	227	73, 530
Breast	33	34.24	96	66, 135
All genital organs	17	23.77	72	42, 115
Cervix uteri	2	7.72	26	3, 94
Corpus uteri	5	4.26	117	38, 274
All uterus	7	12.48	56	22, 116
Other genital organs	10	11.20	89	43, 164
Bladder	1	1.16	86	1, 478
Kidney	5	1.96	255	82, 595
Eye	0	0.12	0	0,2981
Brain/CNS	4	4.24	94	25, 241
Thyroid	0	0.42	0	0, 875
All lymphopoietic	8	11.67	69	30, 135
Lymphosarcoma	1	2.55	39	1, 218
Hodgkins	1	1.52	66	1, 367
Leukemia	4	4.53	88	24, 226
Other lymphatic	2	2.93	68	8, 247
Benign	2	2.57	78	9, 281
Mental disorders	5	1.97	253	82, 591
All circulatory	104	155.28	67	55, 81
All respiratory	22	18.55	119	74, 180
All digestive	17	23.71	72	42, 115
All genito-urinary	4	7.11	56	15, 144
Senility and ill defined	6	4.77	126	46, 274
All injuries	41	36.25	113	81, 153
All accidents	27	22.27	121	80, 176
Motor vehicle accidents	14	12.24	114	62, 192
Suicide	11	10.24	107	54, 192
Cancer residual	8	9.29	86	

contributed after the EOS. The categories of "ever radiation" and "never radiation" are mutually exclusive and collectively exhaustive.

Table 25 presents the characteristics for persons who were ever a radiation worker and those who were never a radiation worker between 1943 and 1981. A significantly elevated SMR for kidney cancer was observed among the subcohort never working with radiation. Five cases were observed compared with 1.46 expected resulting in an SMR of 343 (95% CI = 111, 801). Among radiation workers (Table 26) mortality from all causes, all cancers, all digestive cancers (borderline), all circulatory diseases was significantly less than expected based on US death rates. SMRs for many causes of death such as digestive cancers, colon cancer, lymphopoietic cancers, and lung cancers were less than 100, although 95% confidence intervals were wide and included 100. Only one standardized mortality ratio, deaths due to suicide, significantly exceeded 100. Standardized mortality ratios for skin cancer, ovarian cancer, leukemia, benign neoplasms, mental disorders, and senility/ill defined conditions exceeded 100, although these standardized mortality ratios were nonsignificant.

In order to overcome the Healthy Worker Effect inherent in standardized mortality analyses, maximum likelihood estimates of the rate ratio were calculated to compare cancer mortality among radiation workers with cancer mortality among nonradiation workers within the same cohort. Rate ratios were calculated for 0, 2, 5, 10, 15, 20, and 25 years induction. Table 27 presents rate ratios for the 0 year induction period. No cancer specific rate ratio was significantly elevated, but the following ratios exceeded 1.00: pancreatic cancer

TABLE 25

CHARACTERISTICS OF RADIATION AND NONRADIATION WORKERS: 0 YEARS INDUCTION

	Ever Radiation Worker	Never Radiation Worker
Total persons	1591	3643
Total person-years	29762.2	76922.1
Total number deceased	81	246
Average age of entry	29.31	28.47
Average year of entry	1962.24	1957.96
Average age of death	54.78	57.41
Average year of death	1973.3	1972.38
Average length of follow-up	18.71	21.12
Crude mortality rate (per 100,000 person-years)	272.16	319.80

TABLE 26

STANDARDIZED MORTALITY RATIOS FOR WHITE FEMALES
EMPLOYED AT LEAST SIX MONTHS WHO WERE EVER
EXPOSED OR MONITORED FOR RADIATION:
1943-1981, 0 YEARS INDUCTION

Cause (ICD)	Observed	Expected	SMR	95% CI
All causes	81	105.68	77	61, 95
All cancers	24	36.01	67	43, 99
Oral cancer	0	0.51	0	0, 721
All digestive	2	7.24	28	3, 100
Esophagus	0	0.27	0	0, 1362
Stomach	0	0.90	0	0, 406
Large intestine	1	3.19	31	0, 174
Rectum	0	0.74	0	0, 497
Liver and gallbladder	0	0.62	0	0, 592
Pancreas	1	1.30	77	1, 429
All respiratory	3	4.60	65	13, 190
Larynx	0	0.11	0	0, 3281
Lung	3	4.42	68	14, 198
Bone	0	0.14	0	0, 2710
Skin	1	0.60	167	2, 928
Breast	7	9.20	76	30, 157
All genital organs	5	6.22	80	26, 188
Cervix uteri	0	2.07	0	0, 177
Corpus uteri	1	1.07	93	1, 520
All uterus	1	3.24	31	0, 172
Other genital organs	4	2.96	135	36, 346
Bladder	0	0.28	0	0, 1331
Kidney	0	0.50	0	0, 727
Eye	0	0.03	0	0,11779
Brain/CNS	1	1.15	87	1, 485
Thyroid	0	0.10	0	0, 3532
All lymphopoietic	2	3.04	66	7, 238
Lymphosarcoma	0	0.66	0	0, 554
Hodgkins	0	0.41	0	0, 900
Leukemia	2	1.18	169	19, 611
Other lymphatic	0	0.75	0	0, 488
Benign	1	0.67	149	2, 832
Mental disorders	2	0.53	374	42, 1350
All circulatory	23	35.94	64	41, 96
All respiratory	3	4.63	65	13, 189
All digestive	5	6.25	80	26, 187
All genito-urinary	0	1.75	0	0, 210
Senility and ill defined	3	1.27	236	47, 689
All injuries	16	10.05	159	91, 259
All accidents	6	6.06	99	36, 216
Motor vehicle accidents	3	3.40	88	18, 258
Suicide	8	2.91	275	118, 542
Cancer residual	3	2.40	125	

TABLE 27

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR RADIATION WORKERS COMPARED WITH NONRADIATION WORKERS, 1943-1981, LIMITED TO WORKERS EMPLOYED AT LEAST SIX MONTHS, 0 YEARS INDUCTION

Cause	Ever Radiation Worker (2976.2 Pyrs)	Never Radiation Worker (76922.0 Pyrs)	RR	95% CI
All causes	81	246	0.99	0.76, 1.27
All cancers	24	88	0.77	0.49, 1.21
Oral cancer	0	2	0.00	0.00, 8.97
All digestive	2	13	0.41	0.09, 1.83
Esophagus	0	1	0.00	0.00,49.11
Stomach	0	1	0.00	0.00,49.11
Large intestine	1	8	0.33	0.04, 2.64
Rectum	0	1	0.00	0.00,49.11
Liver and gallbladder	0	1	0.00	0.00,49.11
Pancreas	1	1	2.59	0.16,41.38
All respiratory	3	11	0.77	0.21, 2.76
Lung	3	11	0.77	0.21, 2.76
Skin	1	4	0.72	0.08, 6.53
Breast	7	26	0.74	0.32, 1.71
All genital organs	5	12	1.19	0.42, 3.40
Cervix uteri	0	2	0.00	0.00, 8.97
Corpus uteri	1	4	0.71	0.08, 6.43
All uterus	1	6	0.45	0.05, 3.74
Ovary	4	6	1.99	0.55, 7.14
Bladder	0	1	0.00	0.00,49.11
Kidney	0	5	0.00	0.00, 2.12
Brain/CNS	1	3	0.96	0.10, 9.36
All lymphopoietic	2	6	0.96	0.19, 4.81
Lymphosarcoma	0	1	0.00	0.00,49.11
Hodgkins	0	1	0.00	0.00,49.11
Leukemia	2	2	2.95	0.40,21.75
Other lymphatic	0	2	0.00	0.00, 8.97
Benign	1	1	2.59	0.16,41.58

(RR = 2.59, 95% CI = 0.16, 41.38), ovarian cancer (RR = 1.99, 95% CI = 0.55, 7.14), cancers of the genital organs (RR = 1.19, 95% CI = 0.42, 3.40), and leukemia (RR = 2.95, 95% CI = 0.40, 21.75). No rate ratios were significantly less than expected but ratios for all cancer (RR = 0.77, 95% CI = 0.49, 1.21), all digestive cancer (RR = 0.41, 95% CI = 0.09, 1.83), colon cancer (RR = 0.33, 95% CI = 0.04, 2.64), lung cancer (RR = 0.77, 95% CI = 0.21, 2.76), skin cancer (RR = 0.72, 95% CI = 0.08, 6.53), breast cancer (RR = 0.74, 95% CI = 0.32, 1.71), uterine cancer (RR = 0.71, 95% CI = 0.08, 6.43), and cancers of the cervix and corpus uteri combined (RR = 0.45, 95% CI = 0.05, 3.74) were less than 1.00. Rate ratios for all causes (RR = 0.99, 95% CI = 0.76, 1.27), brain cancers (RR = 0.96, 95% CI = 0.10, 9.36), and all lymphopoietic cancers (RR = 0.96, 95% CI = 0.19, 4.81) were very close to 1.00. No cases of cancers of the bone or thyroid were observed.

Results of the rate ratio analyses at two years induction (Table 28) were very similar to those with no restriction for induction time. No rate ratio was significantly elevated. Rate ratios for cancer of the pancreas (RR = 2.59, 95% CI = 0.16, 41.36), cancer of the ovary (RR = 2.02, 95% CI = 0.56, 7.24), leukemia (RR = 2.97, 95% CI = 0.40, 21.89), and benign neoplasms (RR = 2.60, 95% CI = 0.16, 41.75) exceeded two, but the confidence intervals were wide and included 1.00. Rate ratios for digestive cancer (RR = 0.42, 95% CI = 0.09, 1.84), cancer of the colon (RR = 0.33, 95% CI = 0.04, 2.64), cancer of the cervix or uterus (RR = 0.45, 95% CI = 0.05, 3.75) were quite low, although these deficits were not significant. The rate

TABLE 28

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR RADIATION WORKERS COMPARED WITH NONRADIATION WORKERS, 1943-1981, LIMITED TO WORKERS EMPLOYED AT LEAST SIX MONTHS, 2 YEARS INDUCTION

	Observed			
Cause	Ever Radiation Worker (2976.2 Pyrs)	Never Radiation Worker (76922.0 Pyrs)	RR	95% CI
All causes	81	241	1.01	0.78, 1.31
All cancers	24	87	0.78	0.49, 1.22
Oral cancer	0	2	0.00	0.00, 9.08
All digestive	2	13	0.42	0.09, 1.84
Esophagus	0	1	0.00	0.00,49.70
Stomach	0	1	0.00	0.00,49.70
Large intestine	1	8	0.33	0.04, 2.64
Rectum	0	1	0.00	0.00,49.70
Liver and gallbladder	0	1	0.00	0.00,49.70
Pancreas	1	1	2.59	0.16,41.36
All respiratory	3	11	0.77	0.21, 2.76
Lung	3	11	0.77	0.21, 2.76
Skin	1	4	0.72	0.08, 6.54
Breast	7	26	0.74	0.32, 1.71
All genital organs	5	12	1.20	0.42, 3.43
Cervix uteri	0	2	0.00	0.00, 9.08
Corpus uteri	1	4	0.71	0.08, 6.43
All uterus	1	6	0.45	0.05, 3.75
Ovary	4	6	2.02	0.56, 7.24
Bladder	0	1	0.00	0.00,49.70
Kidney	0	4	0.00	0.00, 2.92
Brain/CNS	1	3	0.98	0.10, 9.57
All lymphopoietic	2	6	0.96	0.19, 4.83
Lymphosarcoma	0	1	0.00	0.00,49.70
Hodgkins	0	1	0.00	0.00,49.70
Leukemia	2	2	2.97	0.40,21.89
Other lymphatic	0	2	0.00	0.00, 9.08
Benign	1	1	2.60	0.16,41.75

ratio for all causes of death was right at expected (RR = 1.01, 95% CI = 0.78, 1.31). Rate ratios for other sites were not remarkable.

At five years induction (Table 29), the rate ratio for all causes was 1.05 (95% CI = 0.81, 1.36) and the ratio for all cancers was 0.76 (95% CI = 0.47, 1.22). No rate ratios were significantly elevated. Rate ratios for cancer of the pancreas (RR = 2.60, 95% CI = 0.16, 41.48), ovary (RR = 2.10, 95% CI = 0.59, 7.55), leukemia (RR = 1.76, 95% CI = 0.16, 19.81) and benign neoplasms (RR = 2.64, 95% CI = 0.17, 42.32) were elevated, but these results were not significant.

At 10 years induction (Table 30), none of the cancer-specific rate ratios were significantly elevated. As with five years induction, cancer of the pancreas, cancer of the ovary, leukemias, and benign neoplasms were nonsignificantly elevated.

No rate ratio was elevated when rate ratios comparing radiation and nonradiation workers were calculated for 15 years induction (Table 31). Rate ratios for cancer of the pancreas (RR = 2.75, 95% CI = 0.17, 44.03), cancer of the ovary (RR = 3.30, 95% CI = 0.65, 16.71), leukemias (RR = 1.99, 95% CI = 0.18, 22.45) and benign neoplasms (RR = 3.04, 95% CI = 0.19, 48.65) were near or exceeded 2.00. Confidence intervals for these rate ratios were wide and included 1.00. Ratios for digestive cancer (RR = 0.57, 95% CI = 0.13, 2.61), colon cancer (RR = 0.40, 95% CI= 0.05, 3.26), cancer of the cervix and corpus uteri (RR = 0.55, 95% CI = 0.06, 4.76), and all lymphopoietic cancer (RR = 0.55, 95% CI = 0.07, 4.58) were considerably below 1.00 but these deficits were nonsignificant.

TABLE 29

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR RADIATION WORKERS COMPARED WITH NONRADIATION WORKERS, 1943-1981, LIMITED TO WORKERS EMPLOYED AT LEAST SIX MONTHS, 5 YEARS INDUCTION

Cause	Observed		RR	95% CI
	Ever Radiation Worker (22776.7 Pyrs)	Never Radiation Worker (61518.4 Pyrs)		
All causes	79	230	1.05	0.81, 1.36
All cancers	22	83	0.76	0.47, 1.22
Oral cancer	0	1	0.00	0.00,51.32
All digestive	2	13	0.42	0.09, 1.86
Esophagus	0	1	0.00	0.00,51.32
Stomach	0	1	0.00	0.00,51.32
Large intestine	1	8	0.33	0.04, 2.67
Rectum	0	1	0.00	0.00,51.32
Liver and gallbladder	0	1	0.00	0.00,51.32
Pancreas	1	1	2.60	0.16,41.48
All respiratory	3	11	0.77	0.21, 2.77
Lung	3	11	0.77	0.21, 2.77
Skin	1	4	0.72	0.08, 6.54
Breast	7	25	0.78	0.34, 1.82
All genital organs	5	11	1.36	0.47, 3.95
Cervix uteri	0	1	0.00	0.00,51.32
Corpus uteri	1	4	0.71	0.08, 6.43
All uterus	1	5	0.55	0.06, 4.76
Ovary	4	6	2.10	0.59, 7.55
Bladder	0	1	0.00	0.00,51.32
Kidney	0	3	0.00	0.00, 4.63
Brain/CNS	0	3	0.00	0.00, 4.63
All lymphopoietic	1	6	0.52	0.06, 4.34
Lymphosarcoma	0	1	0.00	0.00,51.32
Hodgkins	0	1	0.00	0.00,51.32
Leukemia	1	2	1.76	0.16,19.81
Other lymphatic	0	2	0.00	0.00, 9.38
Benign	1	1	2.64	0.17,42.32

TABLE 30

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR RADIATION WORKERS COMPARED WITH NONRADIATION WORKERS, 1943-1981, LIMITED TO WORKERS EMPLOYED AT LEAST SIX MONTHS, 10 YEARS INDUCTION

	Observed			
Cause	Ever Radiation Worker (16671.4 Pyrs)	Never Radiation Worker (46995.4 Pyrs)	RR	95% CI
All causes	75	208	1.13	0.86, 1.47
All cancers	21	72	0.86	0.52, 1.40
Oral cancer	0	1	0.00	0.00,53.56
All digestive	2	12	0.47	0.10, 2.08
Esophagus	0	1	0.00	0.00,53.56
Stomach	0	1	0.00	0.00,53.56
Large intestine	1	7	0.39	0.05, 3.14
Rectum	0	1	0.00	0.00,53.56
Liver and gallbladder	0	1	0.00	0.00,53.56
Pancreas	1	1	2.62	0.16,41.93
All respiratory	3	11	0.77	0.21, 2.78
Lung	3	11	0.77	0.21, 2.78
Skin	1	4	0.99	0.10, 9.65
Breast	7	20	1.03	0.43, 2.45
All genital organs	4	8	3.34	0.66,16.93
Cervix uteri	0	1	0.00	0.00,53.56
Corpus uteri	1	4	0.72	0.08, 6.48
All uterus	1	5	0.56	0.07, 4.81
Ovary	3	3	3.34	0.66,16.93
Bladder	0	1	0.00	0.00,53.56
Kidney	0	2	0.00	0.00, 9.79
Brain/CNS	0	2	0.00	0.00, 9.79
All lymphopoietic	1	6	0.53	0.06, 4.46
Lymphosarcoma	0	1	0.00	0.00,53.56
Hodgkins	0	1	0.00	0.00,53.56
Leukemia	1	2	1.90	0.17,21.43
Other lymphatic	0	2	0.00	0.00, 9.79
Benign	1	1	2.72	0.17,43.55

TABLE 31

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR RADIATION WORKERS COMPARED WITH NONRADIATION WORKERS, 1943-1981, LIMITED TO WORKERS EMPLOYED AT LEAST SIX MONTHS, 15 YEARS INDUCTION

Cause	Observed Ever Radiation Worker (11665.9 Pyrs)	Observed Never Radiation Worker (34291.4 Pyrs)	RR	95% CI
All causes	66	181	1.17	0.88, 1.56
All cancers	19	67	0.85	0.51, 1.42
Oral cancer	0	1	0.00	0.00,55.85
All digestive	2	10	0.57	0.13, 2.61
Esophagus	0	1	0.00	0.00,55.85
Large intestine	1	7	0.40	0.05, 3.26
Rectum	0	1	0.00	0.00,55.85
Pancreas	1	1	2.75	0.17,44.03
All respiratory	3	11	0.80	0.22, 2.87
Lung	3	11	0.80	0.22, 2.87
Skin	1	4	0.73	0.08, 6.60
Breast	5	17	0.90	0.33, 2.44
All genital organs	4	8	1.50	0.45, 5.03
Cervix uteri	0	1	0.00	0.00,55.85
Corpus uteri	1	4	0.70	0.08, 6.29
All uterus	1	5	0.55	0.06, 4.76
Ovary	3	3	3.30	0.65,16.71
Bladder	0	1	0.00	0.00,55.85
Kidney	0	2	0.00	0.00,10.21
Brain/CNS	0	2	0.00	0.00,10.21
All Lymphopoietic	1	6	0.55	0.07, 4.58
Lymphosarcoma	0	1	0.00	0.00,55.85
Hodgkins	0	1	0.00	0.00,55.85
Leukemia	1	2	1.99	0.18,22.45
Other lymphatic	0	2	0.00	0.00,10.21
Benign	1	1	3.04	0.19,48.65

At 20 years induction (Table 32), no significantly elevated or deficit rate ratios were observed. Ratios for cancer of the pancreas (RR = 3.03, 95% CI = 0.19, 48.49) and ovary (RR = 3.51, 95% CI = 0.70, 17.68) remained high, while the ratio for digestive cancer (RR = 0.37, 95% CI = 0.05, 2.92) remained low. None of these ratios were significantly different from 1.00.

At 25 years induction (Table 33), there were 37 deaths, including 12 from cancer, observed among radiation workers. The overall rate ratio for all causes of death was 1.30 (95% CI = 0.89, 1.89). No significantly elevated or deficit rate ratios were observed. The ratio for all cancers (RR = 0.92, 95% CI = 0.49, 1.75) approached 1.00.

Ever Monitored for External Radiation Compared With Never Monitored

Cause-specific standardized mortality ratios were computed for white females ever monitored for external radiation. This subcohort included women employed at least six months who ever wore a film badge or a TLD. Because film badges were not used until 1944, persons terminating before May 18, 1944, were eliminated from the analyses. Table 34 presents the characteristics of both the monitored and nonmonitored subcohort.

Among monitored workers the standardized mortality ratios (Table 35) for all causes and all cancers were 86 (95% CI = 66, 109) and 80 (95% CI = 50, 123), respectively. Only the SMR for suicide (SMR = 350, 95% CI = 140, 720) was significantly elevated. No significant deficits in mortality were observed. Again, among

TABLE 32

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR RADIATION WORKERS COMPARED WITH NONRADIATION WORKERS, 1943-1981, LIMITED TO WORKERS EMPLOYED AT LEAST SIX MONTHS, 20 YEARS INDUCTION

Cause	Observed: Ever Radiation Worker (7447.6 Pyrs)	Observed: Never Radiation Worker (23135.6 Pyrs)	RR	95% CI
All causes	52	151	1.16	0.85, 1.60
All cancers	15	58	0.82	0.46, 1.46
Oral cancer	0	1	0.00	0.00,59.03
All digestive	1	8	0.37	0.05, 2.92
Esophagus	0	1	0.00	0.00,59.03
Large intestine	0	6	0.00	0.00, 2.01
Pancreas	1	1	3.03	0.19,48.49
All respiratory	2	9	0.71	0.15, 3.30
Lung	2	9	0.71	0.15, 3.30
Skin	1	4	1.05	0.11,10.25
Breast	5	15	1.10	0.40, 3.04
All genital organs	4	8	1.67	0.50, 5.60
Cervix uteri	0	1	0.00	0.00,59.03
Corpus uteri	1	4	0.80	0.09, 7.28
All uterus	1	5	0.63	0.07, 5.47
Ovary	3	3	3.51	0.70,17.68
Bladder	0	1	0.00	0.00,59.03
Kidney	0	1	0.00	0.00,59.03
Brain/CNS	0	2	0.00	0.00,10.79
All lymphopoietic	0	4	0.00	0.00, 3.46
Lymphosarcoma	0	1	0.00	0.00,59.03
Hodgkins	0	1	0.00	0.00,59.03
Leukemia	0	1	0.00	0.00,59.03
Other lymphatic	0	1	0.00	0.00,59.03
Benign	0	0	--	----

TABLE 33

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR RADIATION WORKERS COMPARED WITH NONRADIATION WORKERS, 1943-1981, LIMITED TO WORKERS EMPLOYED AT LEAST SIX MONTHS, 25 YEARS INDUCTION

Cause	Observed: Ever Radiation Worker (4017.8 Pyrs)	Observed: Never Radiation Worker (13551.0 Pyrs)	RR	95% CI
All causes	37	105	1.30	0.89, 1.89
All cancers	12	46	0.92	0.49, 1.75
Oral cancer	0	1	0.00	0.00,64.09
All digestive	1	8	0.41	0.05, 3.28
Esophagus	0	1	0.00	0.00,64.09
Large intestine	0	6	0.00	0.00, 2.18
Pancreas	1	1	3.48	0.22,55.74
All respiratory	1	6	0.59	0.07, 4.91
Lung	1	6	0.59	0.07, 4.91
Skin	1	3	1.19	0.12,11.91
Breast	5	11	1.79	0.61, 5.23
All genital organs	3	6	1.87	0.46, 7.60
Cervix uteri	0	1	0.00	0.00,64.09
Corpus uteri	1	2	1.44	0.13,15.91
All uterus	1	3	1.01	0.11, 9.75
Ovary	2	3	3.02	0.49,18.49
Bladder	0	1	0.00	0.00,64.09
Kidney	0	1	0.00	0.00,64.09
Brain/CNS	0	2	0.00	0.00,11.71
All lymphopoietic	0	4	0.00	0.00, 3.76
Lymphosarcoma	0	1	0.00	0.00,64.09
Hodgkins	0	1	0.00	0.00,64.09
Leukemia	0	1	0.00	0.00,64.09
Other lymphatic	0	1	0.00	0.00,64.09
Benign	0	0	--	----

TABLE 34

CHARACTERISTICS OF WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS BETWEEN 1944 AND 1981, EVER MONITORED AND NEVER MONITORED FOR EXPOSURE TO EXTERNAL IONIZING RADIATION, 0 YEARS INDUCTION

	Ever Monitored	Never Monitored
Total persons	1412	4750
Total person-years	19554.5	85977.5
Total number deceased	65	257
Average age of entry	33.17	28.66
Average age of death	54.40	57.37
Average year of death	1974.01	1972.38
Average length of follow-up (years)	13.85	18.10
Crude mortality rate (per 100,000 person-years)	332.40	298.9

TABLE 35

STANDARDIZED MORTALITY RATIOS FOR WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS AND EVER MONITORED FOR EXTERNAL IONIZING RADIATION: 1944-1981, 0 YEARS INDUCTION

Cause	Observed	Expected	SMR	95% CI
All causes	65	75.68	86	66, 109
All cancers	21	26.13	80	50, 123
Oral cancer	0	0.38	0	0, 974
All digestive	2	5.31	38	4, 136
Esophagus	0	0.20	0	0, 1817
Stomach	0	0.65	0	0, 567
Large intestine	1	2.35	43	1, 237
Rectum	0	0.53	0	0, 689
Liver and gallbladder	0	0.45	0	0, 815
Pancreas	1	0.97	103	1, 573
All respiratory	3	3.47	86	17, 253
Larynx	0	0.08	0	0, 4385
Lung	3	3.33	90	18, 263
Bone	0	0.09	0	0, 4002
Skin	1	0.43	235	3, 1308
Breast	7	6.66	105	42, 217
All genital organs	5	4.39	114	37, 266
Cervix uteri	0	1.42	0	0, 258
Corpus uteri	1	0.77	129	2, 719
All uterus	1	2.23	45	1, 250
Other genital organs	4	2.15	186	50, 476
Bladder	0	0.20	0	0, 1800
Kidney	0	0.37	0	0, 983
Eye	0	0.02	0	0,16391
Brain/CNS	0	0.82	0	0, 449
Thyroid	0	0.08	0	0, 4861
All lymphopoietic	1	2.17	46	1, 257
Lymphosarcoma	0	0.48	0	0, 770
Hodgkins	0	0.27	0	0, 1374
Leukemia	1	0.83	121	2, 671
Other lymphatic	0	0.56	0	0, 650
Benign	1	0.45	225	3, 1250
Mental disorders	1	0.38	261	3, 1451
All circulatory	17	26.31	65	38, 103
All respiratory	3	3.34	90	18, 263
All digestive	5	4.44	113	36, 263
All genito-urinary	0	1.15	0	0, 319
Senility and ill defined	3	0.92	326	65, 952
All injuries	12	6.85	175	90, 306
All accidents	4	4.09	98	26, 251
Motor vehicle accidents	3	2.26	133	27, 389
Suicide	7	2.00	350	140, 720
Cancer residual	2	1.75	114	

nonmonitored workers the kidney cancer (SMR = 321, 95% CI = 103, 748) was borderline significant. None of five kidney cancer deaths had been monitored for external ionizing radiation exposure.

When mortality rates for the monitored subcohort were compared with those for the never monitored (Table 36), no rate ratio was significantly elevated. Ratios for cancer of the pancreas (RR = 3.71, 95% CI = 0.23, 59.39), ovary (RR = 3.19, 95% CI = 0.89, 11.46) and benign neoplasms (RR = 4.12, 95% CI = 0.26, 65.84) exceeded 3.00, but the confidence intervals were wide and included 1.00. Ratios for digestive (RR = 0.67, 95% CI = 0.15, 2.98), colon (RR = 0.54, 95% CI = 0.07, 4.37), and lymphopoietic (RR = 0.55, 95% CI = 0.07, 4.53) cancers were low, but these deficits were not significant. Otherwise, ratios were close to expected. No cases of cancers of the bone or thyroid were observed.

When a two-year induction period was incorporated, rate ratios (Table 37) for most causes of death remained the same or increased only slightly. The ratio for cancer of the ovary (RR = 3.62, 95% CI = 0.99, 13.20) was borderline significant.

When an induction time of 5 years (Table 38) was incorporated into the analyses, estimates of the rate ratio generally increased. The rate ratio for cancer of the ovary (RR = 4.52, 95% CI = 1.18, 17.28) significantly exceeded 1.00. Although nonsignificant, ratios for cancer of the pancreas (RR = 4.13, 95% CI = 0.26, 66.13) and benign neoplasms (RR = 4.90, 95% CI = 0.31, 78.30) exceeded 4.00.

Rate ratios generally continued to increase at 10 years induction (Table 39). The ratio for all causes (RR = 1.35,

TABLE 36

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS COMPARING EVER MONITORED FOR EXTERNAL RADIATION WITH NEVER MONITORED: 1944-1981, 0 YEARS INDUCTION

	Observed			
Cause	Ever Radiation Worker (19554.5 Pyrs)	Never Radiation Worker (85977.4 Pyrs)	RR	95% CI
All causes	65	257	1.12	0.85, 1.47
All cancers	21	90	0.96	0.60, 1.55
Oral cancer	0	2	0.00	0.00,15.27
All digestive	2	12	0.67	0.15, 2.98
Esophagus	0	1	0.00	0.00,83.54
Stomach	0	1	0.00	0.00,83.54
Large intestine	1	7	0.54	0.07, 4.37
Rectum	0	1	0.00	0.00,83.54
Liver and gallbladder	0	1	0.00	0.00,83.54
Pancreas	1	1	3.71	0.23,59.39
All respiratory	3	11	1.06	0.30, 3.82
Lung	3	11	1.06	0.30, 3.82
Skin	1	4	1.04	0.12, 9.39
Breast	7	26	1.07	0.46, 2.48
All genital organs	5	12	1.84	0.64, 5.27
Cervix uteri	0	2	0.00	0.00,15.27
Corpus uteri	1	4	0.96	0.11, 8.79
All uterus	1	6	0.66	0.08, 5.53
Ovary	4	6	3.19	0.89,11.46
Bladder	0	1	0.00	0.00,83.54
Kidney	0	5	0.00	0.00, 3.61
Brain/CNS	0	4	0.00	0.00, 4.90
All lymphopoietic	1	7	0.55	0.07, 4.53
Lymphosarcoma	0	1	0.00	0.00,83.54
Hodgkins	0	1	0.00	0.00,83.54
Leukemia	1	3	1.32	0.13,13.23
Other lymphatic	0	2	0.00	0.00,15.27
Benign	1	1	4.12	0.26,65.84

TABLE 37

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS COMPARING EVER MONITORED FOR EXTERNAL RADIATION WITH NEVER MONITORED: 1944-1981, 2 YEARS INDUCTION

	Observed			
Cause	Ever Radiation Worker (16957.5 Pyrs)	Never Radiation Worker (85547.4 Pyrs)	RR	95% CI
All causes	62	260	1.13	0.85, 1.49
All cancers	20	91	0.96	0.59, 1.56
Oral cancer	0	2	0.00	0.00,18.14
All digestive	2	12	0.70	0.16, 3.14
Esophagus	0	1	0.00	0.00,99.25
Stomach	0	1	0.00	0.00,99.25
Large intestine	1	7	0.56	0.07, 4.56
Rectum	0	1	0.00	0.00,99.25
Liver and gallbladder	0	1	0.00	0.00,99.25
Pancreas	1	1	3.87	0.24,61.87
All respiratory	3	11	1.09	0.30, 3.93
Lung	3	11	1.09	0.30, 3.93
Skin	1	4	1.06	0.12, 9.51
Breast	7	26	1.14	0.49, 2.63
All genital organs	5	12	2.01	0.70, 5.79
Cervix uteri	0	2	0.00	0.00,18.14
Corpus uteri	1	4	1.00	0.11, 9.08
All uterus	1	6	0.69	0.08, 5.81
Ovary	4	6	3.62	0.99,13.20
Bladder	0	1	0.00	0.00,99.25
Kidney	0	5	0.00	0.00, 4.29
Brain/CNS	0	4	0.00	0.00, 5.82
All lymphopoietic	0	8	0.00	0.00, 2.37
Lymphosarcoma	0	1	0.00	0.00,99.25
Hodgkins	0	1	0.00	0.00,99.25
Leukemia	0	4	0.00	0.00, 5.82
Other lymphatic	0	2	0.00	0.00,18.14
Benign	1	1	4.26	0.27,68.12

TABLE 38

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS COMPARING EVER MONITORED FOR EXTERNAL RADIATION WITH NEVER MONITORED: 1944-1981, 5 YEARS INDUCTION

	Observed			
Cause	Ever Radiation Worker (13527.4 Pyrs)	Never Radiation Worker (92004.5 Pyrs)	RR	95% CI
All causes	60	262	1.20	0.90, 1.60
All cancers	20	91	1.06	0.65, 1.73
Oral cancer	0	2	0.00	0.00, 23.62
All digestive	2	12	0.76	0.17, 3.43
Esophagus	0	1	0.00	0.00,129.23
Stomach	0	1	0.00	0.00,129.23
Large intestine	1	7	0.60	0.07, 4.89
Rectum	0	1	0.00	0.00,129.23
Liver and gallbladder	0	1	0.00	0.00,129.23
Pancreas	1	1	4.13	0.26, 66.13
All respiratory	3	11	1.14	0.32, 4.11
Lung	3	11	1.14	0.32, 4.11
Skin	1	4	1.07	0.12, 9.68
Breast	7	26	1.26	0.54, 2.92
All genital organs	5	12	2.33	0.80, 6.81
Cervix uteri	0	2	0.00	0.00, 23.62
Corpus uteri	1	4	1.05	0.12, 9.59
All uterus	1	6	0.76	0.09, 6.40
Ovary	4	6	4.52	1.18, 17.28
Bladder	0	1	0.00	0.00,129.23
Kidney	0	5	0.00	0.00, 115.58
Brain/CNS	0	4	0.00	0.00, 7.58
All lymphopoietic	0	8	0.00	0.00, 3.09
Lymphosarcoma	0	1	0.00	0.00,129.23
Hodgkins	0	1	0.00	0.00,129.23
Leukemia	0	4	0.00	0.00, 7.58
Other lymphatic	0	2	0.00	0.00, 123.62
Benign	1	1	4.90	0.31, 78.30

TABLE 39

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS COMPARING EVER MONITORED FOR EXTERNAL RADIATION WITH NEVER MONITORED: 1944-1981, 10 YEARS INDUCTION

	Observed			
Cause	Ever Radiation Worker (9312.5 Pyrs)	Never Radiation Worker (96219.4 Pyrs)	RR	95% CI
All causes	56	266	1.35	1.00, 1.81
All cancers	19	92	1.19	0.72, 1.97
Oral cancer	0	2	0.00	0.00, 35.88
All digestive	2	12	0.93	0.21, 4.23
Esophagus	0	1	0.00	0.00,196.32
Stomach	0	1	0.00	0.00,196.32
Large intestine	1	7	0.69	0.08, 5.64
Rectum	0	1	0.00	0.00,196.32
Liver and gallbladder	0	1	0.00	0.00,196.32
Pancreas	1	1	4.78	0.30, 76.51
All respiratory	3	11	1.27	0.35, 4.60
Lung	3	11	1.27	0.35, 4.60
Skin	1	4	1.15	0.13, 10.32
Breast	7	26	1.52	0.65, 3.54
All genital organs	4	13	2.11	0.66, 6.80
Cervix uteri	0	2	0.00	0.00, 35.88
Corpus uteri	1	4	1.18	0.13, 10.79
All uterus	1	6	0.93	0.11, 8.05
Ovary	3	7	3.52	0.83, 14.97
Bladder	0	1	0.00	0.00,196.32
Kidney	0	5	0.00	0.00, 8.48
Brain/CNS	0	4	0.00	0.00, 11.52
All lymphopoietic	0	8	0.00	0.00, 4.69
Lymphosarcoma	0	1	0.00	0.00,196.32
Hodgkins	0	1	0.00	0.00,196.32
Leukemia	0	4	0.00	0.00, 11.52
Other lymphatic	0	2	0.00	0.00, 35.88
Benign	1	1	6.91	0.43,110.57

95% CI = 1.00, 1.81) was borderline significant. Although still in excess of 3.00, the ratio for ovarian cancer (RR = 3.52, 95% CI = 0.83, 14.97) was no longer statistically significant at the 95% confidence level. Ratios for pancreatic cancer (RR = 4.78, 95% CI = 0.30, 76.51) and benign neoplasms (RR = 6.91, 95% CI = 0.43, 110.57) remained high, but the confidence intervals were wide and the point estimates were not significantly different from 1.00.

At 15 years induction (Table 40), the rate ratio for all causes of death (RR = 1.34, 95% CI = 0.97, 1.87) was borderline significant. Although not statistically significant, rate ratios exceeded 1.00 for most causes of death for which both exposed and unexposed deaths were observed. The exception was the ratio for cancer of the colon (RR = 0.84, 95% CI = 0.11, 6.96). The ratios for cancer of the pancreas (RR = 6.43, 95% CI = 0.40, 104.08) and cancer of the ovary (RR = 2.54, 95% CI = 0.49, 13.08) were the highest, but the confidence intervals included 1.00.

At 20 years induction (Table 41), no rate ratios were significantly elevated. No significant deficits were observed. The rate ratio for cancer of the pancreas was 10.61 (95% CI = 0.65, 174.45), but the confidence interval was very wide and included 1.00.

At 25 years induction (Table 42), the rate ratio for cancer of the pancreas (RR = 36.59, 95% CI = 1.68, 795.25) was significantly elevated. In all instances where both exposed and unexposed cases were observed, the point estimate of the rate ratio exceeded 1.00. However, confidence intervals were wide and included 1.00; therefore, these ratios were not significantly elevated.

TABLE 40

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS COMPARING EVER MONITORED FOR EXTERNAL RADIATION WITH NEVER MONITORED: 1944-1981, 15 YEARS INDUCTION

Cause	Observed: Ever Radiation Worker (19554.5 Pyrs)	Observed: Never Radiation Worker (85977.4 Pyrs)	RR	95% CI
All causes	44	278	1.34	0.97, 1.87
All cancers	15	96	1.16	0.67, 2.03
Oral cancer	0	2	0.00	0.00, 58.99
All digestive	2	12	1.22	0.26, 5.63
Esophagus	0	1	0.00	0.00,322.82
Stomach	0	1	0.00	0.00,322.82
Large intestine	1	7	0.84	0.10, 6.96
Rectum	0	1	0.00	0.00,322.82
Liver and gallbladder	0	1	0.00	0.00,322.82
Pancreas	1	1	6.43	0.40,104.08
All respiratory	3	11	1.63	0.45, 5.90
Lung	3	11	1.63	0.45, 5.90
Skin	1	4	1.40	0.16, 12.71
Breast	4	29	1.03	0.36, 2.96
All genital organs	3	14	1.86	0.51, 6.85
Cervix uteri	0	2	0.00	0.00, 58.99
Corpus uteri	1	4	1.43	0.15, 13.36
All uterus	1	6	1.19	0.14, 10.52
Ovary	2	8	2.54	0.49, 13.08
Bladder	0	1	0.00	0.00,322.82
Kidney	0	5	0.00	0.00, 13.94
Brain/CNS	0	4	0.00	0.00, 18.94
All lymphopoietic	0	8	0.00	0.00, 7.72
Lymphosarcoma	0	1	0.00	0.00,322.82
Hodgkins	0	1	0.00	0.00,322.82
Leukemia	0	4	0.00	0.00, 18.94
Other lymphatic	0	2	0.00	0.00, 58.99
Benign	0	2	0.00	0.00, 58.99

TABLE 41

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS COMPARING EVER MONITORED FOR EXTERNAL RADIATION WITH NEVER MONITORED: 1944-1981, 20 YEARS INDUCTION

Cause	Observed: Ever Radiation Worker (3158.4 Pyrs)	Observed: Never Radiation Worker (102373.5 Pyrs)	RR	95% CI
All causes	29	293	1.30	0.88, 1.93
All cancers	8	103	0.87	0.42, 1.81
Oral cancer	0	2	0.00	0.00,112.56
All digestive	1	13	0.82	0.11, 6.47
Esophagus	0	1	0.00	0.00,615.92
Stomach	0	1	0.00	0.00,615.92
Large intestine	0	8	0.00	0.00, 14.72
Rectum	0	1	0.00	0.00,615.92
Liver and gallbladder	0	1	0.00	0.00,615.92
Pancreas	1	1	10.61	0.65,174.45
All respiratory	1	13	0.70	0.09, 5.42
Lung	1	13	0.70	0.09, 5.42
Skin	0	5	0.00	0.00, 26.60
Breast	3	30	1.17	0.35, 3.89
All genital organs	2	15	1.78	0.38, 8.21
Cervix uteri	0	2	0.00	0.00,112.56
Corpus uteri	1	4	2.17	0.23, 20.97
All uterus	1	6	1.89	0.21, 17.26
Ovary	1	9	1.68	0.20, 14.09
Bladder	0	1	0.00	0.00,615.92
Kidney	0	5	0.00	0.00, 26.60
Brain/CNS	0	4	0.00	0.00, 36.14
All lymphopoietic	0	8	0.00	0.00, 14.72
Lymphosarcoma	0	1	0.00	0.00,615.92
Hodgkins	0	1	0.00	0.00,615.92
Leukemia	0	4	0.00	0.00, 36.14
Other lymphatic	0	2	0.00	0.00,112.56
Benign	0	2	0.00	0.00,112.56

TABLE 42

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS COMPARING EVER MONITORED FOR EXTERNAL RADIATION WITH NEVER MONITORED: 1944-1981, 25 YEARS INDUCTION

	Observed			
Cause	Ever Radiation Worker (1311.2 Pyrs)	Never Radiation Worker (104220.7 Pyrs)	RR	95% CI
All causes	16	306	1.40	0.84, 2.36
All cancers	5	106	1.09	0.44, 2.73
Oral cancer	0	2	0.00	0.00, 276.02
All digestive	1	13	1.59	0.20, 12.82
Esophagus	0	1	0.00	0.00,1510.43
Stomach	0	1	0.00	0.00,1510.43
Large intestine	0	8	0.00	0.00, 36.11
Rectum	0	1	0.00	0.00,1510.43
Liver and gallbladder	0	1	0.00	0.00,1510.43
Pancreas	1	1	36.59	1.68, 795.25
All respiratory	1	13	1.38	0.18, 10.89
Lung	1	13	1.38	0.18, 10.89
Skin	0	5	0.00	0.00, 65.23
Breast	2	31	1.73	0.40, 7.49
All genital organs	1	16	1.92	0.23, 15.83
Cervix uteri	0	2	0.00	0.00, 276.02
Corpus uteri	1	4	4.50	0.42, 48.44
All uterus	1	6	4.33	0.41, 45.52
Ovary	0	10	0.00	0.00, 27.77
Bladder	0	1	0.00	0.00,1510.43
Kidney	0	5	0.00	0.00, 65.23
Brain/CNS	0	4	0.00	0.00, 88.62
All lymphopoietic	0	8	0.00	0.00, 36.11
Lymphosarcoma	0	1	0.00	0.00,1510.43
Hodgkins	0	1	0.00	0.00,1510.43
Leukemia	0	4	0.00	0.00, 88.62
Other lymphatic	0	2	0.00	0.00, 276.02
Benign	0	2	0.00	0.00, 276.02

Cumulative External Radiation Dose: At Least 1 Rem Compared With Less Than 1 Rem

The next analyses concerned women with cumulative radiation doses of at least 1 rem, between 1944 and 1981. Again, because external radiation monitoring did not begin until May 18, 1944, persons terminating before this date were omitted. Analyses were limited to white women employed at least six months. Table 43 presents the characteristics of women with cumulative radiation exposures of at least 1 rem and those for women monitored but with cumulative exposures of less than 1 rem.

Table 44 presents standardized mortality ratios for women with cumulative radiation doses of at least 1 rem. Only 12 deaths were observed among these women, with only 4 deaths due to cancer. These cancer deaths included: one breast cancer (SMR = 119, 95% CI = 2, 663), one ovarian cancer (SMR = 366, 95% CI = 5, 2039), one leukemia (SMR = 1043, 95% CI = 14, 5805), and one residual cancer (SMR = 466). The residual cancer was an ICDA-8 171, which is a malignant neoplasm of connective soft tissue. The death certificate stated the cause of death as "metastatic hemangiopericytoma". Although the SMRs for the site-specific cancers exceeded 100, the confidence intervals were wide and included 100; therefore, these SMRs were not significantly elevated. SMRs for all causes (SMR = 135, 95% CI = 69, 235) and all cancers (SMR = 123, 95% CI = 33, 315) were not significantly elevated. Only the SMR for suicide at 928 (95% CI = 104, 3352) was significantly elevated. No significantly elevated SMRs were observed for workers with cumulative exposures of less than 1 rem.

TABLE 43

CHARACTERISTICS OF THE WHITE FEMALES MONITORED FOR EXTERNAL RADIATION WITH CUMULATIVE RADIATION DOSES OF ≥1 REM AND <1 REM

	≥1 REM	<1 REM
Total persons	120	1404
Total person-years	2056.2	17498.3
Total number deceased	12	53
Average age of entry	35.51	33.17
Average year of entry	1963.93	1967.43
Average age of death	56.38	53.95
Average year of death	1974.95	1973.80
Average length of follow-up (years)	17.13	12.46
Crude mortality rate (per 100,000 person-years)	583.60	302.89

TABLE 44

STANDARDIZED MORTALITY RATIOS FOR WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS WITH CUMULATIVE RADIATION DOSES OF $\geq$1 REM BETWEEN 1943 AND 1981, 0 YEARS INDUCTION

Cause	Observed	Expected	SMR	95% CI
All causes	12	8.92	135	69, 235
All cancers	4	3.25	123	33, 315
Oral cancer	0	0.05	0	0, 7507
All digestive	0	0.65	0	0, 564
Esophagus	0	0.03	0	0, 14123
Stomach	0	0.08	0	0, 4622
Large intestine	0	0.29	0	0, 1283
Rectum	0	0.07	0	0, 5498
Liver and gallbladder	0	0.05	0	0, 6739
Pancreas	0	0.12	0	0, 3084
All respiratory	0	0.44	0	0, 834
Larynx	0	0.01	0	0, 33162
Lung	0	0.42	0	0, 868
Bone	0	0.01	0	0, 34142
Skin	0	0.05	0	0, 7507
Breast	1	0.84	119	2, 663
All genital organs	1	0.56	178	2, 993
Cervix uteri	0	0.18	0	0, 2008
Corpus uteri	0	0.10	0	0, 3766
All uterus	0	0.29	0	0, 1284
Other genital organs	1	0.27	366	5, 2039
Bladder	0	0.02	0	0, 15312
Kidney	0	0.05	0	0, 8038
Eye	0	0.00	0	0,134249
Brain/CNS	0	0.10	0	0, 3669
Thyroid	0	0.01	0	0, 40707
All lymphopoietic	1	0.25	392	5, 2183
Lymphosarcoma	0	0.06	0	0, 6201
Hodgkins	0	0.03	0	0, 12173
Leukemia	1	0.10	1043	14, 5805
Other lymphatic	0	0.07	0	0, 5441
Benign	0	0.06	0	0, 6589
Mental disorders	0	0.04	0	0, 8186
All circulatory	5	2.99	167	54, 391
All respiratory	0	0.39	0	0, 931
All digestive	0	0.55	0	0, 667
All genito-urinary	0	0.14	0	0, 2629
Senility and ill defined	0	0.10	0	0, 3546
All injuries	3	0.72	418	84, 1222
All accidents	0	0.43	0	0, 848
Motor vehicle accidents	0	0.23	0	0, 1600
Suicide	2	0.22	928	104, 3352
Cancer residual	1	0.21	466	

Maximum likelihood estimates of the rate ratio, comparing rates for workers with cumulative radiation doses of at least 1 rem with workers with cumulative radiation doses of less than 1 rem, were calculated. The calculations were limited to white females employed between 1944 and 1979 and exposed between 1944 and 1981. Persons terminating before May 18, 1944 were excluded. Only workers employed at least six months were included in the analyses.

Rate ratios were calculated for all causes and cancer-specific causes for 0, 2, 5, 10, 15, and 20 years induction. The 25-year induction period contained too few deaths (n=4) to justify calculating rate ratios.

As stated above, only 12 deaths, 4 from cancer, were observed among workers with cumulative radiation doses of at least 1 rem at 0 years induction. A total of 53 deaths, 17 from cancer, were observed among workers with cumulative radiation doses of less than 1 rem. Analyses were restricted to individuals actually monitored for external radiation exposure. Table 45 presents cancer-specific rate ratios comparing workers with cumulative doses of at least 1 rem with workers with doses of less than 1 rem. The rate ratios for all causes (RR = 1.81, 95% CI = 0.95, 3.45) and all cancers (RR = 1.54, 95% CI = 0.51, 4.62) were nonsignificantly elevated. Rate ratios were only calculated for cancers of the breast (RR = 1.06, 95% CI = 0.13, 8.95) and cancers of the ovary (RR = 1.82, 95% CI = 0.19, 17.51). No unexposed deaths were observed for leukemia; therefore, the rate ratio could not be calculated. The 95% confidence interval indicated a lower bound of 0.45 for leukemia.

TABLE 45

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO COMPARING WORKERS WITH CUMULATIVE RADIATION DOSES OF ≥1 REM WITH WORKERS WITH CUMULATIVE DOSES <1 REM, 1944-1981, LIMITED TO WORKERS EMPLOYED AT LEAST SIX MONTHS, 0 YEARS INDUCTION

Cause	Observed: Exposed (2056.2 Pyrs)	Observed: Not Exposed (17498.3 Pyrs)	RR	95% CI
All causes	12	53	1.81	0.95, 3.45
All cancers	4	17	1.54	0.51, 4.62
All digestive	0	2	0.00	0.00, 29.55
Large intestine	0	1	0.00	0.00,161.70
Pancreas	0	1	0.00	0.00,161.70
All respiratory	0	3	0.00	0.00, 14.59
Lung	0	3	0.00	0.00, 14.59
Skin	0	1	0.00	0.00,161.70
Breast	1	6	1.06	0.13, 8.95
All genital organs	1	4	1.34	0.15, 11.99
Corpus uteri	0	1	0.00	0.00,161.70
All uterus	0	1	0.00	0.00,161.70
Ovary	1	3	1.82	0.19, 17.51
All lymphopoietic	1	0	--	0.45, ---
Leukemia	1	0	--	0.45, ---
Benign	0	1	0.00	0.00,161.70

At two years induction (Table 46), rate ratios for all causes and all cancers were 1.73 (95% CI = 0.89, 3.37) and 1.13 (95% CI = 0.33, 3.86), respectively. Ratios for cancer of the breast (RR = 1.12, 95% CI = 0.13, 9.39) and ovary (RR = 1.88, 95% CI = 0.20, 18.17) exceeded 1.00, but the associated 95% confidence intervals were wide and included 1.00. The rate ratio for leukemia could not be calculated, but the upper bound of the confidence limit was 183.8.

At five years induction (Table 47), rate ratios for all causes (RR = 1.69, 95% CI = 0.85, 3.38) and all cancers (RR = 0.76, 95% CI = 0.18, 3.28) declined compared with those observed at two years induction (Table 46). Conversely, rate ratios for cancers of the breast (RR = 1.19, 95% CI = 0.14, 10.04) and ovary (RR = 2.13, 95% CI = 0.22, 20.60) increased, but were not statistically significant. The upper bound of the confidence interval for leukemia was 220.58.

When rate ratios for 10 years induction (Table 48) were calculated, the ratio for all causes (RR = 1.98, 95% CI = 0.99, 3.97) was borderline significant. The rate ratio for all cancers (RR = 0.85, 95% CI = 0.20, 3.70) was less than expected, but this deficit was not statistically significant. Rate ratios for cancers of the breast (RR = 1.27, 95% CI = 0.15, 10.65) and ovary (RR = 2.69, 95% CI = 0.27, 27.06) were not significantly elevated.

Table 49 presents maximum likelihood estimates for the rate ratio for selected causes of death at 15 years induction. The rate ratio for all causes of death was significantly elevated at 2.14 (95% CI = 1.03, 4.45). The rate ratio for all cancers was very close to the expected value at 0.99 (95% CI = 0.23, 4.30). Rate ratios for cancers

TABLE 46

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO COMPARING WORKERS WITH CUMULATIVE RADIATION DOSES OF ≥1 REM WITH WORKERS WITH CUMULATIVE DOSES OF <1 REM, 1944-1981, LIMITED TO WORKERS EMPLOYED AT LEAST SIX MONTHS, 2 YEARS INDUCTION

Cause	Exposed (1832.3 Pyrs)	Not Exposed (17722.2 Pyrs)	RR	95% CI
All causes	11	54	1.73	0.89, 3.37
All cancers	3	18	1.13	0.33, 3.86
All digestive	0	2	0.00	0.00, 33.59
Large intestine	0	1	0.00	0.00,183.80
Pancreas	0	1	0.00	0.00,183.80
All respiratory	0	3	0.00	0.00, 16.58
Lung	0	3	0.00	0.00, 16.58
Skin	0	1	0.00	0.00,183.80
Breast	1	6	1.12	0.13, 9.39
All genital organs	1	4	1.38	0.15, 12.41
Corpus uteri	0	1	0.00	0.00,183.80
All uterus	0	1	0.00	0.00,183.80
Ovary	1	3	1.88	0.20, 18.17
All lymphopoietic	0	1	0.00	0.00,183.80
Leukemia	0	1	0.00	0.00,183.80
Benign	0	1	0.00	0.00,183.80

TABLE 47

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO COMPARING WORKERS WITH CUMULATIVE RADIATION DOSES OF $\geq$1 REM WITH WORKERS WITH CUMULATIVE DOSES OF <1 REM, 1944-1981, LIMITED TO WORKERS EMPLOYED AT LEAST SIX MONTHS, 5 YEARS INDUCTION

Cause	Observed: Exposed (1551.8 Pyrs)	Observed: Not Exposed (18006.1 Pyrs)	RR	95% CI
All causes	10	55	1.69	0.85, 3.38
All cancers	2	19	0.76	0.18, 3.28
All digestive	0	2	0.00	0.00, 40.31
Large intestine	0	1	0.00	0.00,220.58
Pancreas	0	1	0.00	0.00,220.58
All respiratory	0	3	0.00	0.00, 19.90
Lung	0	3	0.00	0.00, 19.90
Skin	0	1	0.00	0.00,220.58
Breast	1	6	1.19	0.14, 10.04
All genital organs	1	4	1.54	0.17, 13.82
Corpus uteri	0	1	0.00	0.00,220.58
All uterus	0	1	0.00	0.00,220.58
Ovary	1	3	2.13	0.22, 20.60
All lymphopoietic	0	1	0.00	0.00,220.58
Leukemia	0	1	0.00	0.00,220.58
Benign	0	1	0.00	0.00,220.58

TABLE 48

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO COMPARING WORKERS WITH CUMULATIVE RADIATION DOSES OF ≥1 REM WITH WORKERS WITH CUMULATIVE DOSES OF <1 REM, 1944-1981, LIMITED TO WORKERS EMPLOYED AT LEAST SIX MONTHS, 10 YEARS INDUCTION

Cause	Observed: Exposed (1147.7 Pyrs)	Observed: Not Exposed (18406.8 Pyrs)	RR	95% CI
All causes	10	55	1.98	0.99, 3.97
All cancers	2	19	0.85	0.20, 3.70
All digestive	0	2	0.00	0.00, 55.72
Large intestine	0	1	0.00	0.00,304.89
Pancreas	0	1	0.00	0.00,304.89
All respiratory	0	3	0.00	0.00, 27.51
Lung	0	3	0.00	0.00, 27.51
Skin	0	1	0.00	0.00,304.89
Breast	1	6	1.27	0.15, 10.65
All genital organs	1	4	1.86	0.20, 17.17
Corpus uteri	0	1	0.00	0.00,304.89
All uterus	0	1	0.00	0.00,304.89
Ovary	1	3	2.69	0.27, 27.06
All lymphopoietic	0	1	0.00	0.00,304.89
Leukemia	0	1	0.00	0.00,304.89
Benign	0	1	0.00	0.00,304.89

TABLE 49

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO COMPARING WORKERS WITH CUMULATIVE RADIATION DOSES OF ≥1 REM WITH WORKERS WITH CUMULATIVE DOSES OF <1 REM, 1944-1981, LIMITED TO WORKERS EMPLOYED AT LEAST SIX MONTHS, 15 YEARS INDUCTION

	Observed			
Cause	Exposed (820.4 Pyrs)	Not Exposed (18753.6 Pyrs)	RR	95% CI
All causes	9	56	2.14	1.03, 4.45
All cancers	2	19	0.99	0.23, 4.30
All digestive	0	2	0.00	0.00, 79.41
Large intestine	0	1	0.00	0.00,434.52
Pancreas	0	1	0.00	0.00,434.52
All respiratory	0	3	0.00	0.00, 39.21
Lung	0	3	0.00	0.00, 39.21
Skin	0	1	0.00	0.00,434.52
Breast	1	6	1.38	0.17, 11.56
All genital organs	1	4	2.19	0.23, 20.89
Corpus uteri	0	1	0.00	0.00,434.52
All uterus	0	1	0.00	0.00,434.52
Ovary	1	3	3.38	0.31, 36.42
All lymphopoietic	0	1	0.00	0.00,434.52
Leukemia	0	1	0.00	0.00,434.52
Benign	0	1	0.00	0.00,434.52

of the breast (RR = 1.38, 95% CI = 0.17, 11.56) and ovary (RR = 3.38, 95% CI = 0.31, 36.42) exceeded 1.00, but were not significantly greater than 1.00. The upper bound for leukemia was 434.52.

The rate ratio for all causes of death (RR = 2.74, 95% CI = 1.26, 5.95) remained significantly elevated at 20 years induction (Table 50). The ratio for all cancers (RR = 1.46, 95% CI = 0.33, 6.41) exceeded 1.00, but was not significantly elevated. Rate ratios for cancers of the breast (RR = 2.12, 95% CI = 0.25, 18.00) and ovary (RR = 5.66, 95% CI = 0.51, 62.73) exceeded 1.00, but the confidence intervals were wide and these ratios were not statistically significant.

At 25 years induction, insufficient numbers of deaths (n=4) and deaths due to cancer (n=1) and person-years (n=241.9) existed for the white females employed at least six months with cumulative radiation doses of at least 1 rem; therefore, rate ratios were not calculated for this subset. The only cancer death was due to breast cancer (SMR = 534, 95% CI = 7, 2969).

Ever Bioassayed for Plutonium Compared With Never Bioassayed for Plutonium

Analyses were conducted of all white women hired between 1943 and 1979 and ever-bioassayed for plutonium between March 1, 1945, and December 31, 1981. Persons terminating before March 1, 1945, were omitted, because that date represents the start of the plutonium bioassay program at Los Alamos. Persons were considered monitored from the date of their first bioassay (plus induction) until death (if deceased before the EOS), termination (if lost to follow-up), 1980 (if

TABLE 50

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO COMPARING WORKERS WITH CUMULATIVE RADIATION DOSES OF ≥1 REM WITH WORKERS WITH CUMULATIVE DOSES OF <1 REM, 1944-1981, LIMITED TO WORKERS EMPLOYED AT LEAST SIX MONTHS, 20 YEARS INDUCTION

	Observed			
Cause	Exposed (504.3 Pyrs)	Not Exposed (19072.5 Pyrs)	RR	95% CI
All causes	8	57	2.74	1.26, 5.95
All cancers	2	19	1.46	0.33, 6.41
All digestive	0	2	0.00	0.00, 131.39
Large intestine	0	1	0.00	0.00, 718.98
Pancreas	0	1	0.00	0.00, 718.98
All respiratory	0	3	0.00	0.00, 64.88
Lung	0	3	0.00	0.00, 64.88
Skin	0	1	0.00	0.00, 718.98
Breast	1	6	2.12	0.25, 18.00
All genital organs	1	4	3.41	0.35, 33.10
Corpus uteri	0	1	0.00	0.00, 718.98
All uterus	0	1	0.00	0.00, 718.98
Ovary	1	3	5.66	0.51, 62.73
All lymphopoietic	0	1	0.00	0.00, 718.98
Leukemia	0	1	0.00	0.00, 718.98
Benign	0	1	0.00	0.00, 718.98

lost to follow-up but known to be alive in the 1982 SSA return), or EOS. Persons who were not bioassayed before death or EOS remained "never monitored" and left the study at death, termination, 1980, or EOS as described above. If an induction time was employed in the specific analyses, a person must achieve their bioassay date plus induction before entering the "monitored" category. As before, no one was allowed to leave the study after the EOS. Induction periods of 0, 2, 5, 10, 15, 20, and 25 years were employed in these analyses.

Table 51 presents the characteristics for plutonium bioassayed and nonbioassayed workers. Table 52 presents standardized mortality ratios for the subcohort monitored for plutonium with a urine bioassay between 1945 and 1981. This analysis included no restriction for induction time. No SMR was significantly elevated over 100. SMRS for all causes (SMR = 82, 95% CI = 54, 120) and all cancers (SMR = 54, 95% CI = 20, 117) indicated less mortality than expected based on US death rates. Interesting SMRs for cancer-specific sites included corpus uterus (SMR = 293, 95% CI = 4, 1628), brain (SMR = 291, 95% CI = 4, 1618), and leukemia (SMR = 284, 95% CI = 4, 1580). Confidence intervals for all three of these sites were very wide and included 100; therefore, these SMRs were not statistically elevated. Other interesting SMRs were observed for benign neoplasms (SMR = 505, 95% CI = 7, 2812) and mental disorders (SMR = 631, 95% CI = 8, 3509). Again, the confidence intervals were very wide and included 100. No significantly elevated or deficit SMRs were observed in this analysis.

TABLE 51

CHARACTERISTICS OF THE WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS EVER BIOASSAYED AND NEVER BIOASSAYED FOR PLUTONIUM: 1945-1981

	Ever Bioassayed	Never Bioassayed
Total persons	479	4985
Total person-years	7965.7	95253.9
Total number deceased	27	285
Average age of entry	31.81	28.77
Average year of entry	1964.10	1959.49
Average age of death	57.63	56.36
Average year of death	1972.73	1972.60
Average length of follow-up (years)	16.63	19.11
Crude mortality rate (per 100,000 person-years)	338.95	299.20

TABLE 52

STANDARDIZED MORTALITY RATIOS FOR WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS EVER BIOASSAYED FOR PLUTONIUM: 1945-1981, 0 YEARS INDUCTION

Cause	Observed	Expected	SMR	95% CI
All causes	27	32.74	82	54, 120
All cancers	6	11.19	54	20, 117
Oral cancer	0	0.16	0	0, 2268
All digestive	0	2.32	0	0, 158
Esophagus	0	0.09	0	0, 4186
Stomach	0	0.29	0	0, 1281
Large intestine	0	1.02	0	0, 360
Rectum	0	0.24	0	0, 1556
Liver and gallbladder	0	0.20	0	0, 1845
Pancreas	0	0.42	0	0, 874
All respiratory	1	1.45	69	1, 384
Larynx	0	0.04	0	0,10239
Lung	1	1.39	72	1, 400
Bone	0	0.04	0	0, 9117
Skin	0	0.17	0	0, 2103
Breast	0	2.82	0	0, 130
All genital organs	1	1.91	52	1, 291
Cervix uteri	0	0.62	0	0, 592
Corpus uteri	1	0.34	293	4, 1628
All uterus	1	0.98	102	1, 565
Other genital organs	0	0.92	0	0, 397
Bladder	0	0.09	0	0, 4097
Kidney	0	0.16	0	0, 2299
Eye	0	0.01	0	0,37492
Brain/CNS	1	0.34	291	4, 1618
Thyroid	0	0.03	0	0,11131
All lymphopoietic	1	0.92	109	1, 605
Lymphosarcoma	0	0.21	0	0, 1784
Hodgkins	0	0.11	0	0, 3240
Leukemia	1	0.35	284	4, 1580
Other lymphatic	0	0.24	0	0, 1535
Benign	1	0.20	505	7, 2812
Mental disorders	1	0.16	631	8, 3509
All circulatory	11	11.63	95	47, 169
All respiratory	1	1.44	70	1, 387
All digestive	1	1.90	53	1, 292
All genito-urinary	0	0.52	0	0, 699
Senility and ill defined	1	0.38	266	3, 1478
All injuries	3	2.75	109	22, 319
All accidents	2	1.67	119	13, 431
Motor vehicle accidents	0	0.91	0	0, 403
Suicide	1	0.79	126	2, 701
Cancer residual	2	0.75	266	

No significantly elevated SMRs were observed, when the subcohort never bioassayed for plutonium was examined. The SMRs for all causes (77, 95% CI = 69, 87) and circulatory diseases (66, 95% CI = 53, 81) were significantly less than expected.

Maximum likelihood estimates of the rate ratio were calculated which compared mortality rates for the plutonium "bioassayed" directly with rates for the "nonbioassayed". Person-years and deaths in these analyses were allocated in the identical fashion as in the SMR analyses described above.

Table 53 presents rate ratios for bioassayed compared with nonbioassayed women, with zero years induction. The rate ratio for all causes was 1.06 (95% CI = 0.71, 1.57) and for all cancers was 0.63 (95% CI = 0.27, 1.44). No rate ratio was significantly more or less than expected. Rate ratios in excess of 2.00 included corpus uterus (RR = 2.39, 95% CI = 0.27, 21.39), brain/cns (RR = 3.89, 95% CI = 0.40, 37.57), leukemia (RR = 4.31, 95% CI = 0.44, 41.96), and benign neoplasms (RR = 9.76, 95% CI = 0.61, 156.13). Although the point estimates appeared large, confidence intervals were very wide and included the null value of 1.00 in all instances. None of these rate ratios represent a significant increase in deaths in the bioassayed workers compared with the nonbioassayed workers. No bone or thyroid cancers were observed.

At two years induction (Table 54), no significantly elevated or deficit rate ratios were observed. The all causes SMR was right at expected 1.02 (95% CI = 0.68, 1.54) while the all cancer rate ratio was less than half of expected at 0.43 (95% CI = 0.16, 1.17). The rate

TABLE 53

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS EVER BIOASSAYED FOR PLUTONIUM COMPARED WITH FEMALES NEVER BIOASSAYED: 1945-1981, 0 YEARS INDUCTION

	Observed			
Cause	Ever Bioassayed (7965.7 Pyrs)	Never Bioassayed (95253.8 Pyrs)	RR	95% CI
All causes	27	285	1.06	0.71, 1.57
All cancers	6	100	0.63	0.28, 1.44
Oral cancer	0	2	0.00	0.00, 41.52
All digestive	0	12	0.00	0.00, 3.39
Stomach	0	1	0.00	0.00,227.22
Large intestine	0	7	0.00	0.00, 6.39
Rectum	0	1	0.00	0.00,227.22
Liver and gallbladder	0	1	0.00	0.00,227.22
Pancreas	0	2	0.00	0.00, 41.52
All respiratory	1	13	0.83	0.11, 6.35
Lung	1	13	0.83	0.11, 6.35
Skin	0	3	0.00	0.00, 20.50
Breast	0	32	0.00	0.00, 1.17
All genital organs	1	16	0.64	0.09, 4.83
Cervix uteri	0	2	0.00	0.00, 41.52
Corpus uteri	1	4	2.39	0.27, 21.39
All uterus	1	6	1.62	0.20, 13.46
Ovary	0	10	0.00	0.00, 4.18
Bladder	0	1	0.00	0.00,227.22
Kidney	0	5	0.00	0.00, 9.81
Brain/CNS	1	3	3.89	0.40, 37.57
All lymphopoietic	1	7	1.63	0.20, 13.36
Lymphosarcoma	0	1	0.00	0.00,227.22
Hodgkins	0	1	0.00	0.00,227.22
Leukemia	1	3	4.31	0.44, 41.96
Other lymphatic	0	2	0.00	0.00, 41.52
Benign	1	1	9.76	0.61,156.13

TABLE 54

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS EVER BIOASSAYED FOR PLUTONIUM COMPARED WITH FEMALES NEVER BIOASSAYED: 1945-1981, 2 YEARS INDUCTION

	Observed			
Cause	Ever Bioassayed (7086.2 Pyrs)	Never Bioassayed (96133.2 Pyrs)	RR	95% CI
All causes	25	287	1.02	0.68, 1.54
All cancers	4	102	0.43	0.16, 1.17
Oral cancer	0	2	0.00	0.00, 47.11
All digestive	0	12	0.00	0.00, 3.85
Stomach	0	1	0.00	0.00,257.77
Large intestine	0	7	0.00	0.00, 7.25
Rectum	0	1	0.00	0.00,257.77
Liver and gallbladder	0	1	0.00	0.00,257.77
Pancreas	0	2	0.00	0.00, 47.11
All respiratory	1	13	0.85	0.11, 6.47
Lung	1	13	0.85	0.11, 6.47
Skin	0	3	0.00	0.00, 23.26
Breast	0	32	0.00	0.00, 1.33
All genital organs	1	16	0.67	0.05, 4.32
Cervix uteri	0	2	0.00	0.00, 47.11
Corpus uteri	1	4	2.42	0.27, 21.72
All uterus	1	6	1.66	0.10, 13.69
Ovary	0	10	0.00	0.00, 4.74
Bladder	0	1	0.00	0.00,257.77
Kidney	0	5	0.00	0.00, 11.13
Brain/CNS	0	4	0.00	0.00, 15.12
All lymphopoietic	0	8	0.00	0.00, 6.16
Lymphosarcoma	0	1	0.00	0.00,257.77
Hodgkins	0	1	0.00	0.00,257.77
Leukemia	0	4	0.00	0.00, 15.12
Other lymphatic	0	2	0.00	0.00, 47.11
Benign	1	1	9.94	0.62,159.02

ratio for benign neoplasms was still very large at 9.94 (95% CI = 0.62, 159.02) but this was based on one case in each category (bioassayed and nonbioassayed). This rate ratio for benign neoplasms was not statistically significant.

No significantly elevated or deficit rate ratios were observed at five years induction (Table 55). The rate ratio was 1.11 (95% CI = 0.74, 1.67) for all causes and 0.46 (95% CI = 0.17, 1.25) for all cancers. The rate ratio for benign neoplasms at 10.51 (95% CI = 0.66, 168.08) was large but not significant.

At 10 years induction (Table 56), the rate ratio for all causes was 1.10 (95% CI = 0.71, 1.70). The all cancers rate ratio was 0.52 (95% CI = 0.19, 1.40). No significant elevated or deficit rate ratios were observed, although the point estimate for benign neoplasms (RR = 12.71, 95% CI = 0.80, 203.27) was again quite large.

A significantly elevated rate ratio of 17.36 (95% CI = 1.09, 277.61) was observed for benign neoplasms at 15 years induction. This observation was based on one bioassayed and one nonbioassayed benign neoplasm. The ICDA-8 code for the bioassayed death was 2381, which is a benign neoplasm of the brain. The ICDA-8 code for the nonbioassayed death was 218X, which is a uterine fibroma. Rate ratios were not significantly elevated or reduced for any other cause of death. See Table 57 for the rate ratios at 15 years induction.

No significantly elevated rate ratios were observed at 20 years induction (Table 58). There was no longer a bioassayed death from benign neoplasms. The rate ratio for all causes was 1.17 (95% CI = 0.70, 1.99), while the rate ratio for all cancers remained

TABLE 55

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS EVER BIOASSAYED FOR PLUTONIUM COMPARED WITH FEMALES NEVER BIOASSAYED: 1945-1981, 5 YEARS INDUCTION

Cause	Observed: Ever Bioassayed (5868.2 Pyrs)	Observed: Never Bioassayed (97351.3 Pyrs)	RR	95% CI
All causes	25	287	1.11	0.74, 1.67
All cancers	4	102	0.46	0.17, 1.25
Oral cancer	0	2	0.00	0.00, 57.60
All digestive	0	12	0.00	0.00, 4.70
Stomach	0	1	0.00	0.00,315.21
Large intestine	0	7	0.00	0.00, 8.86
Rectum	0	1	0.00	0.00,315.21
Liver and gallbladder	0	1	0.00	0.00,315.21
Pancreas	0	2	0.00	0.00, 57.60
All respiratory	1	13	0.87	0.11, 6.69
Lung	1	13	0.87	0.11, 6.69
Skin	0	3	0.00	0.00, 28.44
Breast	0	32	0.00	0.00, 1.63
All genital organs	1	16	0.74	0.05, 4.84
Cervix uteri	0	2	0.00	0.00, 57.60
Corpus uteri	1	4	2.49	0.28, 22.35
All uterus	1	6	1.75	0.11, 14.51
Ovary	0	10	0.00	0.00, 5.79
Bladder	0	1	0.00	0.00,315.21
Kidney	0	5	0.00	0.00, 13.61
Brain/CNS	0	4	0.00	0.00, 18.49
All lymphopoietic	0	8	0.00	0.00, 7.54
Lymphosarcoma	0	1	0.00	0.00,315.21
Hodgkins	0	1	0.00	0.00,315.21
Leukemia	0	4	0.00	0.00, 18.49
Other lymphatic	0	2	0.00	0.00, 57.60
Benign	1	1	10.51	0.66,168.08

TABLE 56

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS EVER BIOASSAYED FOR PLUTONIUM COMPARED WITH FEMALES NEVER BIOASSAYED: 1945-1981, 10 YEARS INDUCTION

	Observed			
Cause	Ever Bioassayed (4394.5 Pyrs)	Never Bioassayed (98825.0 Pyrs)	RR	95% CI
All causes	22	290	1.10	0.71, 1.70
All cancers	4	102	0.52	0.19, 1.40
Oral cancer	0	2	0.00	0.00, 78.09
All digestive	0	12	0.00	0.00, 6.38
Stomach	0	1	0.00	0.00,427.33
Large intestine	0	7	0.00	0.00, 12.01
Rectum	0	1	0.00	0.00,427.33
Liver and gallbladder	0	1	0.00	0.00,427.33
Pancreas	0	2	0.00	0.00, 78.09
All respiratory	1	13	0.92	0.12, 7.02
Lung	1	13	0.92	0.12, 7.02
Skin	0	3	0.00	0.00, 38.56
Breast	0	32	0.00	0.00, 2.21
All genital organs	1	16	0.87	0.17, 7.90
Cervix uteri	0	2	0.00	0.00, 78.09
Corpus uteri	1	4	2.62	0.29, 23.49
All uterus	1	6	2.01	0.12, 17.16
Ovary	0	10	0.00	0.00, 7.86
Bladder	0	1	0.00	0.00,427.33
Kidney	0	5	0.00	0.00, 18.46
Brain/CNS	0	4	0.00	0.00, 25.07
All lymphopoietic	0	8	0.00	0.00, 10.22
Lymphosarcoma	0	1	0.00	0.00,427.33
Hodgkins	0	1	0.00	0.00,427.33
Leukemia	0	4	0.00	0.00, 25.07
Other lymphatic	0	2	0.00	0.00, 78.09
Benign	1	1	12.71	0.80,203.27

TABLE 57

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS EVER BIOASSAYED FOR PLUTONIUM COMPARED WITH FEMALES NEVER BIOASSAYED: 1945-1981, 15 YEARS INDUCTION

	Observed			
Cause	Ever Bioassayed (3117.4 Pyrs)	Never Bioassayed (100102.1 Pyrs)	RR	95% CI
All causes	20	292	1.20	0.76, 1.89
All cancers	4	102	0.61	0.22, 1.67
Oral cancer	0	2	0.00	0.00,111.51
All digestive	0	12	0.00	0.00, 9.11
Stomach	0	1	0.00	0.00,610.18
Large intestine	0	7	0.00	0.00, 17.15
Rectum	0	1	0.00	0.00,610.18
Liver and gallbladder	0	1	0.00	0.00,610.18
Pancreas	0	2	0.00	0.00,111.51
All respiratory	1	13	1.01	0.13, 7.76
Lung	1	13	1.01	0.13, 7.76
Skin	0	3	0.00	0.00, 55.06
Breast	0	32	0.00	0.00, 3.15
All genital organs	1	16	1.05	0.20, 11.14
Cervix uteri	0	2	0.00	0.00,111.51
Corpus uteri	1	4	3.06	0.34, 27.43
All uterus	1	6	2.50	0.43, 28.00
Ovary	0	10	0.00	0.00, 11.22
Bladder	0	1	0.00	0.00,610.18
Kidney	0	5	0.00	0.00, 26.35
Brain/CNS	0	4	0.00	0.00, 35.80
All lymphopoietic	0	8	0.00	0.00, 14.59
Lymphosarcoma	0	1	0.00	0.00,610.18
Hodgkins	0	1	0.00	0.00,610.18
Leukemia	0	4	0.00	0.00, 35.80
Other lymphatic	0	2	0.00	0.00,111.51
Benign	1	1	17.36	1.09,277.61

TABLE 58

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS EVER BIOASSAYED FOR PLUTONIUM COMPARED WITH FEMALES NEVER BIOASSAYED: 1945-1981, 20 YEARS INDUCTION

Cause	Observed: Ever Bioassayed (2001.2 Pyrs)	Observed: Never Bioassayed (101218.3 Pyrs)	RR	95% CI
All causes	15	297	1.17	0.70, 1.99
All cancers	3	103	0.59	0.19, 1.87
Oral cancer	0	2	0.00	0.00,175.63
All digestive	0	12	0.00	0.00, 14.34
Stomach	0	1	0.00	0.00,961.09
Large intestine	0	7	0.00	0.00, 27.02
Rectum	0	1	0.00	0.00,961.09
Liver and gallbladder	0	1	0.00	0.00,961.09
Pancreas	0	2	0.00	0.00,175.63
All respiratory	1	13	1.30	0.17, 9.97
Lung	1	13	1.30	0.17, 9.97
Skin	0	3	0.00	0.00, 86.72
Breast	0	32	0.00	0.00, 4.96
All genital organs	1	16	1.46	0.28, 16.95
Cervix uteri	0	2	0.00	0.00,175.63
Corpus uteri	1	4	4.78	0.49, 46.16
All uterus	1	6	3.75	0.62, 50.54
Ovary	0	10	0.00	0.00, 17.67
Bladder	0	1	0.00	0.00,961.09
Kidney	0	5	0.00	0.00, 41.51
Brain/CNS	0	4	0.00	0.00, 56.39
All lymphopoietic	0	8	0.00	0.00, 22.98
Lymphosarcoma	0	1	0.00	0.00,961.09
Hodgkins	0	1	0.00	0.00,961.09
Leukemia	0	4	0.00	0.00, 56.39
Other lymphatic	0	2	0.00	0.00,175.63
Benign	0	2	0.00	0.00,175.63

low at 0.59 (95% CI = 0.19, 1.87). The ratio for cancers of the uterus was 4.77 (95% CI = 0.49, 46.16), but the confidence interval was wide and this ratio was not significant.

At 25 years induction (Table 59), the all causes rate ratio was 0.84 (95% CI = 0.40, 1.80) and the all cancers rate ratio was 0.92 (95% CI = 0.29, 2.92). Only three cancers were observed among the bioassayed group, one lung (RR = 2.08, 95% CI = 0.27, 16.26), one uterine (RR = 6.67, 95% CI = 0.67, 66.65) and one unspecified malignant neoplasm (ICDA-8 199).

Positive Plutonium Uptake Compared With No Positive Plutonium Uptake

The next series of plutonium analyses examined the bioassayed subcohort and calculated SMRS for persons monitored for plutonium with a "positive uptake" and those persons monitored for plutonium with "no positive uptake". Persons entered the study at their first bioassay date or hire year plus six months, whichever was latest. Person-years and deaths occurring up to the first positive sample date plus induction were considered as "no positive uptake", while person-years after the first sample date plus induction contributed to the category "positive uptake." Persons left the study at death, termination, 1980, or EOS, as described before. Persons who did not achieve first bioassay date plus induction before death, loss to follow-up, or EOS only contributed person-years to the "no positive uptake" category. Deaths were counted in an identical fashion as person-years. For example, if an individual died after achieving first bioassay date plus induction but before EOS, her death was counted in the category of

TABLE 59

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS EVER BIOASSAYED FOR PLUTONIUM COMPARED WITH FEMALES NEVER BIOASSAYED: 1945-1981, 25 YEARS INDUCTION

Cause	Ever Bioassayed (1083.7 Pyrs)	Never Bioassayed (102135.8 Pyrs)	RR	95% CI
All causes	7	305	0.84	0.40, 1.80
All cancers	3	103	0.92	0.29, 2.92
Oral cancer	0	2	0.00	0.00, 327.45
All digestive	0	12	0.00	0.00, 26.74
Stomach	0	1	0.00	0.00,1791.84
Large intestine	0	7	0.00	0.00, 50.37
Rectum	0	1	0.00	0.00,1791.84
Liver and gallbladder	0	1	0.00	0.00,1791.84
Pancreas	0	2	0.00	0.00, 327.45
All respiratory	1	13	2.08	0.27, 16.26
Lung	1	13	2.08	0.27, 16.26
Skin	0	3	0.00	0.00, 161.68
Breast	0	32	0.00	0.00, 9.26
All genital organs	1	16	2.31	0.43, 27.28
Cervix uteri	0	2	0.00	0.00, 327.45
Corpus uteri	1	4	6.67	0.67, 66.65
All uterus	1	6	5.66	0.91, 79.51
Ovary	0	10	0.00	0.00, 32.94
Bladder	0	1	0.00	0.00,1791.84
Kidney	0	5	0.00	0.00, 77.39
Brain/CNS	0	4	0.00	0.00, 105.13
All lymphopoietic	0	8	0.00	0.00, 42.84
Lymphosarcoma	0	1	0.00	0.00,1791.84
Hodgkins	0	1	0.00	0.00,1791.84
Leukemia	0	4	0.00	0.00, 105.13
Other lymphatic	0	2	0.00	0.00, 327.45
Benign	0	2	0.00	0.00, 327.45

"positive uptake". No deaths or person-years were counted after the EOS date. Induction times of 0, 2, 5, 10, 15, 20, and 25 years were calculated. Table 60 presents the characteristics for both white females with a positive plutonium uptake at bioassay and those with no positive plutonium uptake at 0 years induction.

Among those with a positive plutonium uptake (Table 61), 23 deaths were observed compared with 22.29 expected (SMR = 103, 95% CI = 65, 155). Six cancer deaths (SMR = 79, 95% CI = 29, 172) were observed. None of the SMRs were significantly greater or less than 100. SMRs observed for cancer-specific sites were: 105 (95% CI = 1, 584) for lung cancer, 428 (95% CI = 6, 2382) for cancer of the uterus, 439 (95% CI = 6, 2443), and 426 (95% CI = 6, 2371) for leukemia. Confidence intervals for SMRs for all these cancer sites were very wide and included 100. Three of these deaths were due to cardiovascular disease and one was due to digestive disease.

Due to the limited number of observed events, only a few rate ratios were calculated comparing women with a positive bioassay with women with a no positive bioassay. Table 62 presents the rate ratio for all causes of deaths at zero years induction. The rate ratio was 2.67 (95% CI = 0.90, 7.92). Although there were six cancer deaths among those with a positive bioassay, there were none among those with no positive bioassay; therefore, no cancer-specific rate ratios were calculated.

Tables 63 through 67 present the all causes and all cancers rate ratios for 2, 5, 10, 15, 20, and 25 years induction. At two years induction (Table 63), the all causes rate ratio was 1.90 (95% CI = 0.74, 4.91) and the all cancer rate ratio was 1.33 (95% CI = 0.23, 7.74).

TABLE 60

CHARACTERISTICS OF THE WHITE FEMALES WITH POSITIVE PLUTONIUM UPTAKE AT BIOASSAY COMPARED TO THOSE WITH NO POSITIVE PLUTONIUM UPTAKE

	Positive Uptake	No Positive Uptake
Total Persons	358	413
Total person-years	4985.4	2980.30
Total number deceased	23	4
Average age of entry	34.03	32.52
Average year of entry	1967.21	1963.08
Average age of death	58.21	54.29
Average year of death	1973.3	1969.49
Average length of follow-up (years)	13.93	7.22
Crude mortality rate (per 100,000 person-years)	461.35	134.21

TABLE 61

STANDARDIZED MORTALITY RATIOS FOR WHITE FEMALES WITH A POSITIVE PLUTONIUM UPTAKE AT BIOASSAY: 1945-1981, 0 YEARS INDUCTION

Cause	Observed	Expected	SMR	95% CI
All causes	23	22.29	103	65, 155
All cancers	6	7.57	79	29, 172
Oral cancer	0	0.11	0	0, 3318
All digestive	0	1.60	0	0, 229
Esophagus	0	0.06	0	0, 6022
Stomach	0	0.20	0	0, 1876
Large intestine	0	0.71	0	0, 520
Rectum	0	0.16	0	0, 2269
Liver and gallbladder	0	0.14	0	0, 2667
Pancreas	0	0.29	0	0, 1249
All respiratory	1	0.99	101	1, 561
Larynx	0	0.02	0	0,14956
Lung	1	0.95	105	1, 584
Bone	0	0.03	0	0,13850
Skin	0	0.12	0	0,3188
Breast	0	1.89	0	0, 194
All genital organs	1	1.27	79	1, 437
Cervix uteri	0	0.40	0	0, 919
Corpus uteri	1	0.23	428	6, 2382
All uterus	1	0.64	155	2, 864
Other genital organs	0	0.62	0	0, 589
Bladder	0	0.06	0	0, 5780
Kidney	0	0.11	0	0, 3338
Eye	0	0.01	0	0,55214
Brain/CNS	1	0.23	439	6, 2443
Thyroid	0	0.02	0	0,16162
All lymphopoietic	1	0.62	162	2, 900
Lymphosarcoma	0	0.14	0	0, 2645
Hodgkins	0	0.07	0	0, 5169
Leukemia	1	0.23	426	6, 2371
Other lymphatic	0	0.17	0	0, 2196
Benign	1	0.13	791	10, 4398
Mental disorders	1	0.11	946	12, 5262
All circulatory	8	8.21	97	42, 192
All respiratory	1	0.98	102	1, 566
All digestive	0	1.27	0	0, 290
All genito-urinary	0	0.34	0	0, 1079
Senility and ill defined	1	0.25	393	5, 2189
All injuries	3	1.78	169	34, 493
All accidents	2	1.08	185	21, 667
Motor vehicle accidents	0	0.58	0	0, 632
Suicide	1	0.51	196	3, 1092
Cancer residual	2	0.51	391	

TABLE 62

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR WHITE FEMALES WITH A POSITIVE PLUTONIUM UPTAKE COMPARED TO THOSE WITH NO POSITIVE PLUTONIUM UPTAKE, BIOASSAYED ONLY: 1945-1981, 0 YEARS INDUCTION

Cause	Observed: Ever Positive Bioassay (4985.4 Pyrs)	Observed: Never Positive Bioassay (2980.3 Pyrs)	RR	95% CI
All causes	23	4	2.67	0.90,7.92
All cancers	6	0	--	0.92, --
All respiratory	1	0	--	0.03, --
Lung	1	0	--	0.03, --
All genital organs	1	0	--	0.03, --
Corpus uteri	1	0	--	0.03, --
All uterus	1	0	--	0.03, --
Brain/CNS	1	0	--	0.03, --
All lymphopoietic	1	0	--	0.03, --
Leukemia	1	0	--	0.03, --
Benign	1	0	--	0.03, --

TABLE 63

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR WHITE FEMALES WITH A POSITIVE PLUTONIUM UPTAKE COMPARED TO THOSE WITH NO POSITIVE PLUTONIUM UPTAKE, BIOASSAYED ONLY: 1945-1981, 2 YEARS INDUCTION

	Observed			
Cause	Ever Positive Bioassay (4322.2 Pyrs)	Never Positive Bioassay (3643.45 Pyrs)	RR	95% CI
All causes	21	6	1.90	0.74, 4.91
All cancers	4	2	1.33	0.23, 7.44
All respiratory	1	0	--	0.04, --
Lung	1	0	--	0.04, --
All genital organs	1	0	--	0.04, --
Corpus uteri	1	0	--	0.04, --
All uterus	1	0	--	0.04, --
Brain/CNS	0	1	0.00	0.00,16.02
All lymphopoietic	0	1	0.00	0.00,16.02
Leukemia	0	1	0.00	0.00,16.02
Benign	1	0	--	0.04, --

The rate ratio for all causes (RR = 2.63, 95% CI = 0.99, 7.00) was borderline significant at five years induction (Table 64). This finding was based on 21 deaths with positive bioassay and 6 deaths with no positive bioassay. The all cancers rate ratio was 2.11 (95% CI = 0.34, 13.34), but this was not significantly elevated.

Table 65 presents the rate ratios for 10 years induction. The all causes rate ratio was 2.11 (95% CI = 0.83, 5.34) and the all cancers rate ratio was 3.58 (95% CI = 0.46, 27.58). Neither of these rate ratios were significantly elevated.

At 15 years induction (Table 66), the rate ratio for all causes of death was borderline significant at 2.54 (95% CI = 0.99, 6.51). This finding was based on 16 positive bioassay deaths and 11 nonpositive bioassay deaths. The rate ratio for all cancers at 8.05 (95% CI = 0.65, 99.27) was quite large, but because the confidence interval was wide and included 1.00 this finding was not statistically significant.

At 20 years induction (Table 67), the rate ratio was not significant for either all causes (RR = 1.72, 95% CI = 0.64, 4.63) or all cancers (RR = 4.11, 95% CI = 0.43, 39.39). At 25 years induction (Table 68), the rate ratio for all causes (RR = 0.58, 95% CI = 0.15, 2.18) no longer exceeded 1.00. Although still greater than 1.00, the rate ratio for all cancers (RR = 2.72, 95% CI = 0.37, 20.11) was not significantly different from 1.00.

TABLE 64

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR WHITE FEMALES WITH A POSITIVE PLUTONIUM UPTAKE COMPARED TO THOSE WITH NO POSITIVE PLUTONIUM UPTAKE,BIOASSAYED ONLY: 1945-1981, 5 YEARS INDUCTION

	Observed			
Cause	Ever Positive Bioassay (3455.3 Pyrs)	Never Positive Bioassay (4510.4 Pyrs)	RR	95% CI
All causes	21	6	2.63	0.99, 7.00
All cancers	4	2	2.11	0.34,13.34
All respiratory	1	0	--	0.07, --
Lung	1	0	--	0.07, --
All genital organs	1	0	--	0.07, --
Corpus uteri	1	0	--	0.07, --
All uterus	1	0	--	0.07, --
Brain/CNS	0	1	0.00	0.00,24.80
All lymphopoietic	0	1	0.00	0.00,24.80
Leukemia	0	1	0.00	0.00,24.80
Benign	1	0	--	0.07, --

TABLE 65

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR WHITE FEMALES WITH A POSITIVE PLUTONIUM UPTAKE COMPARED TO THOSE WITH NO POSITIVE PLUTONIUM UPTAKE, BIOASSAYED ONLY: 1945-1981, 10 YEARS INDUCTION

	Observed			
Cause	Ever Positive Bioassay (2446.3 Pyrs)	Never Positive Bioassay (5519.4 Pyrs)	RR	95% CI
All causes	18	9	2.11	0.83, 5.34
All cancers	4	2	3.58	0.46,27.58
All respiratory	1	0	--	0.12, --
Lung	1	0	--	0.12, --
All genital organs	1	0	--	0.12, --
Corpus uteri	1	0	--	0.12, --
All uterus	1	0	--	0.12, --
Brain/CNS	0	1	0.00	0.00,42.87
All lymphopoietic	0	1	0.00	0.00,42.87
Leukemia	0	1	0.00	0.00,42.87
Benign	1	0	--	0.12, --

TABLE 66

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR WHITE FEMALES WITH A POSITIVE PLUTONIUM UPTAKE COMPARED TO THOSE WITH NO POSITIVE PLUTONIUM UPTAKE, BIOASSAYED ONLY: 1945-1981, 15 YEARS INDUCTION

	Observed			
Cause	Ever Positive Bioassay (1627.0 Pyrs)	Never Positive Bioassay (6338.7 Pyrs)	RR	95% CI
All causes	16	11	2.54	0.99, 6.51
All cancers	4	2	8.05	0.65,99.27
All respiratory	1	0	--	0.21, --
Lung	1	0	--	0.21, --
All genital organs	1	0	--	0.21, --
Corpus uteri	1	0	--	0.21, --
All uterus	1	0	--	0.21, --
Brain/CNS	0	1	0.00	0.00,74.01
All lymphopoietic	0	1	0.00	0.00,74.01
Leukemia	0	1	0.00	0.00,74.01
Benign	1	0	--	0.21, --

TABLE 67

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR WHITE FEMALES WITH A POSITIVE PLUTONIUM UPTAKE COMPARED TO THOSE WITH NO POSITIVE PLUTONIUM UPTAKE, BIOASSAYED ONLY: 1945-1981, 20 YEARS INDUCTION

Cause	Observed: Ever Positive Bioassay (961.0 Pyrs)	Observed: Never Positive Bioassay (7004.7 Pyrs)	RR	95% CI
All causes	10	17	1.72	0.64, 4.63
All cancers	3	3	4.11	0.43, 39.39
All respiratory	1	0	--	0.38, --
Lung	1	0	--	0.38, --
All genital organs	1	0	--	0.38, --
Corpus uteri	1	0	--	0.38, --
All uterus	1	0	--	0.38, --
Brain/CNS	0	1	0.00	0.00,138.48
All lymphopoietic	0	1	0.00	0.00,138.48
Leukemia	0	1	0.00	0.00,138.48
Benign	0	1	0.00	0.00,138.48

TABLE 68

MAXIMUM LIKELIHOOD ESTIMATES OF THE RATE RATIO FOR WHITE FEMALES WITH A POSITIVE PLUTONIUM UPTAKE COMPARED TO THOSE WITH NO POSITIVE PLUTONIUM UPTAKE, BIOASSAYED ONLY: 1945-1981, 25 YEARS INDUCTION

	Observed			
Cause	Ever Positive Bioassay (445.1 Pyrs)	Never Positive Bioassay (7520.6 Pyrs)	RR	95% CI
All causes	3	24	0.57	0.15, 2.18
All cancers	2	4	2.72	0.37, 20.11
All respiratory	1	0	--	0.89, --
Lung	1	0	--	0.89, --
All genital organs	1	0	--	0.89, --
Corpus uteri	1	0	--	0.89, --
All uterus	1	0	--	0.89, --
Brain/CNS	0	1	0.00	0.00,321.08
All lymphopoietic	0	1	0.00	0.00,321.08
Leukemia	0	1	0.00	0.00,321.08
Benign	0	1	0.00	0.00,321.08

Survival Analyses

The results of the survival analyses were severely limited by the large proportion of the cohort with censored survival times (93.5%). As a result of this high proportion of censored observations, estimates of the mean survival time are probably not meaningful. Figure 1 presents the survival curve for all white females employed at least six months.

Probably more meaningful are the comparisons of survival distributions for women in the radiation categories. Figure 2 presents a comparison of survival curves for radiation and nonradiation workers. Both of these subcohorts had high proportions of censored observations with 94.8% of the survival times for the nonradiation workers censored. As would be expected from the graphical display of the data, both the Breslow statistic (1.309, 1 d.f., $p = 0.2526$) and the Mantel-Cox statistic (0.296, 1 d.f., $p = 0.5864$) indicated no significant difference in survival for the two groups. Figure 3 shows the comparison for women monitored for external ionizing radiation compared with survival for women never monitored for external ionizing radiation. These comparisons were limited to white women employed at least six months and employed on or after May 18, 1944. Both visual and statistical examination of these subcohorts revealed no difference in survival for the monitored and nonmonitored women. The values for the Breslow (1.902, 1 d.f., $p = 0.1679$) and the Mantel-Cox (0.161, 1 d.f., $p = 0.6885$) were not statistically significant. Finally, Figure 4 presents a comparison of survival for women bioassayed for plutonium compared with women never bioassayed for plutonium.

FIGURE 1

CUMULATIVE PROPORTION SURVIVING FOR WHITE FEMALES
EMPLOYED AT LEAST SIX MONTHS

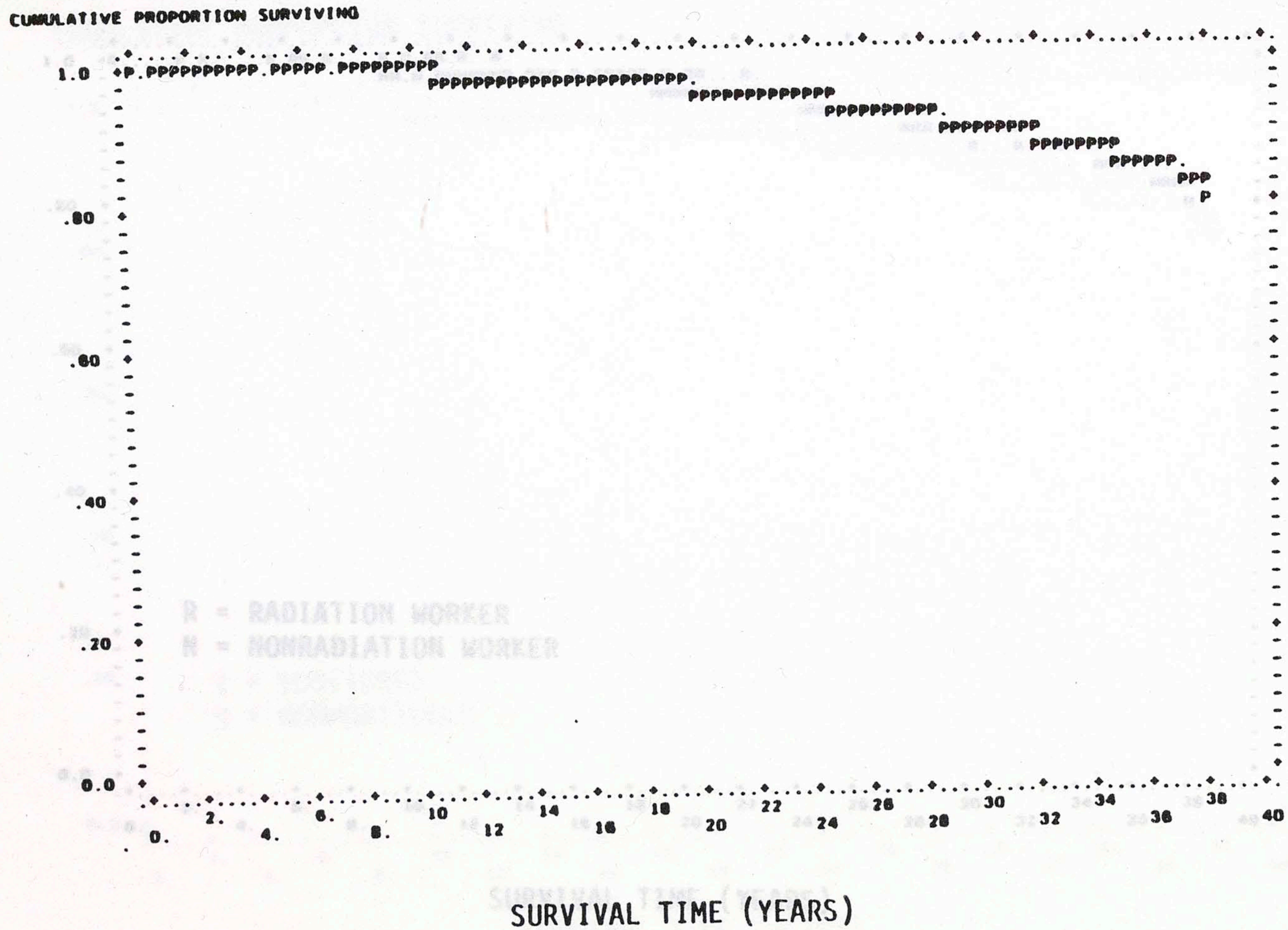
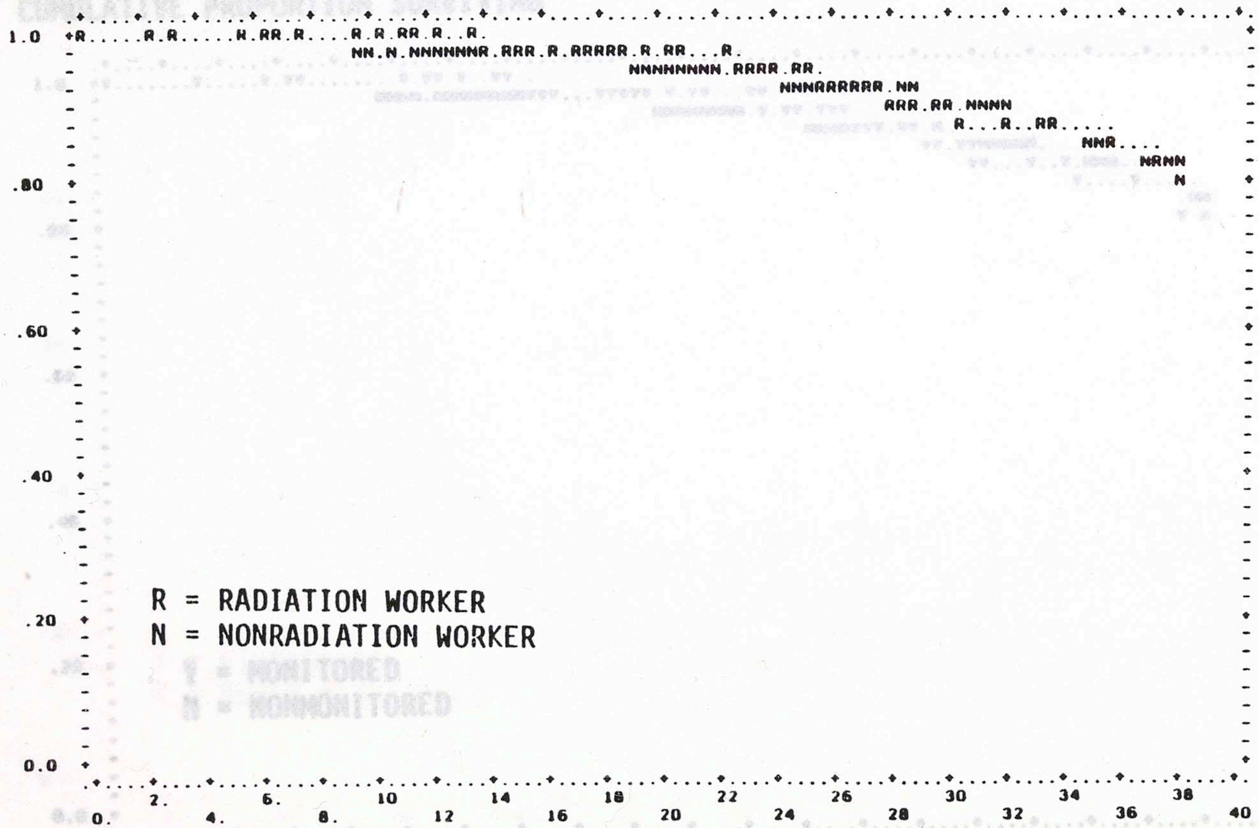


FIGURE 2

A COMPARISON OF THE CUMULATIVE PROPORTION SURVIVING FOR WHITE FEMALE RADIATION AND NONRADIATION WORKERS

CUMULATIVE PROPORTION SURVIVING

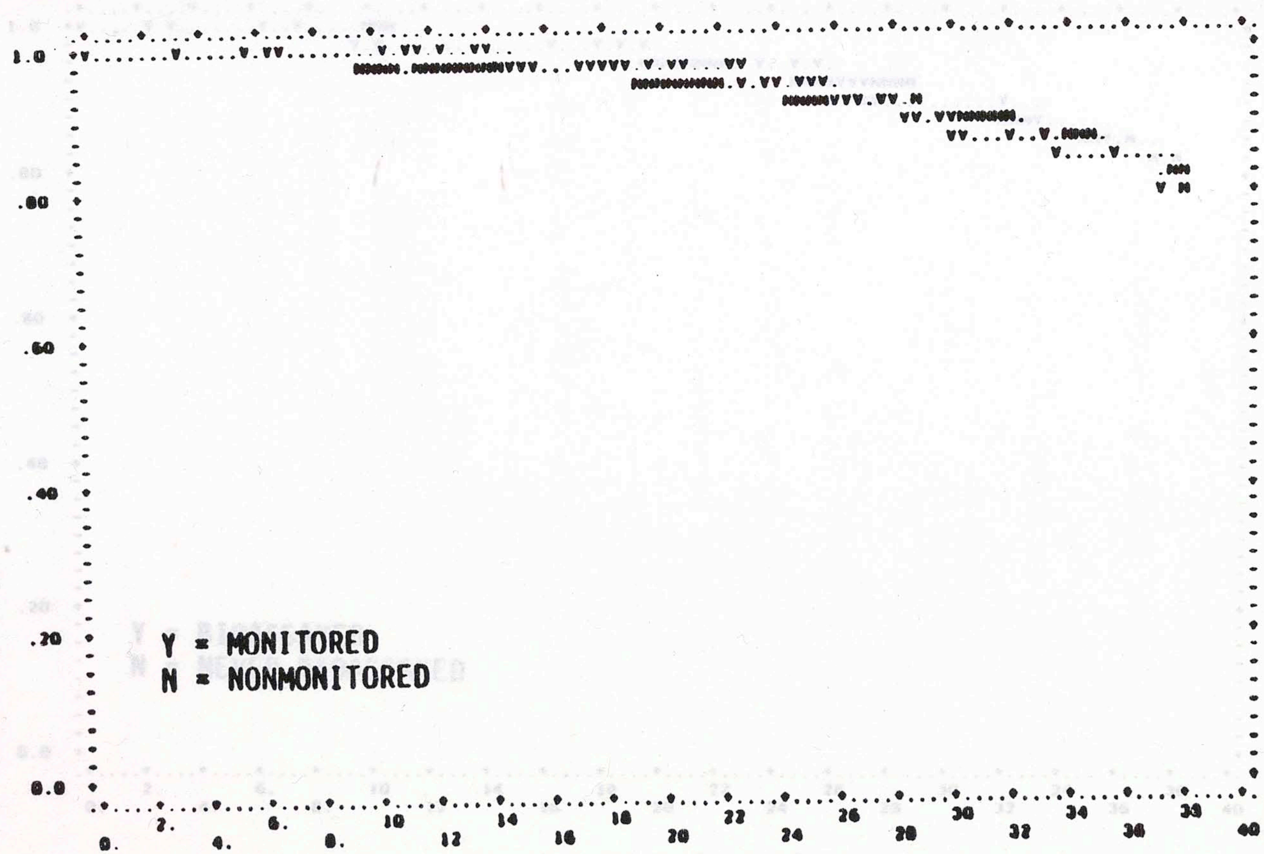


SURVIVAL TIME (YEARS)

FIGURE 3

A COMPARISON OF THE CUMULATIVE PROPORTION SURVIVING FOR WHITE FEMALES MONITORED FOR EXTERNAL IONIZING AND NOT MONITORED FOR EXTERNAL IONIZING RADIATION

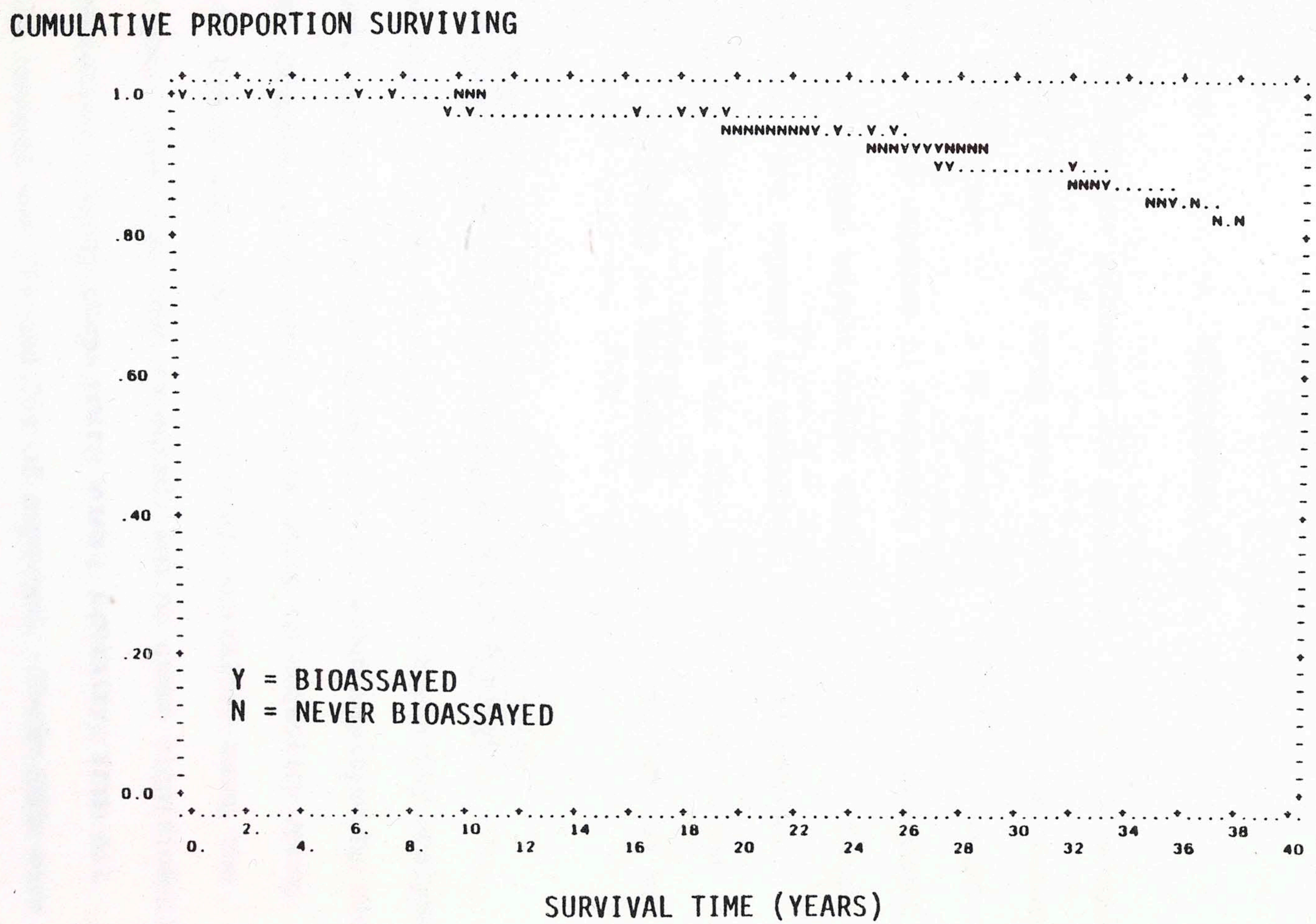
CUMULATIVE PROPORTION SURVIVING



SURVIVAL TIME (YEARS)

FIGURE 4

A COMPARISON OF THE CUMULATIVE PROPORTION SURVIVING FOR WHITE FEMALES BIOASSAYED FOR PLUTONIUM AND THOSE NEVER BIOASSAYED FOR PLUTONIUM



Approximately 94% of the survival times were censored in both groups. The survival curves for these two groups were not statistically different based on either the Breslow (0.146, 1 d.f., $p = 0.7020$) or the Mantel-Cox (0.193, 1 d.f., $p = 0.6602$) statistics.

CHAPTER VI

DISCUSSION

This investigation addressed two questions. First, it sought to determine whether mortality among women employed by the Laboratory resembled that among women in the US population. Second, it sought to determine whether women exposed to radiation during their employment at the Laboratory experienced higher cancer mortality rates than female Laboratory employees not exposed to radiation. Survival between radiation and nonradiation workers was also compared. Due to the limited number of nonwhites in the cohort, analyses were limited to white females.

Comparison of Mortality Among Los Alamos White Females With Mortality Among US White Females

To address the first question, standardized mortality analyses were conducted. Mortality observed among white women employed by the Laboratory was compared to expected values based on mortality among white women in the US population. In general, mortality among the white female cohort was less than expected, and no cause significantly exceeded expectation. Among these white women, mortality from all causes and all cancers was 76% and 78% of expected. These SMRs were significantly low and probably represent the impact of the healthy worker effect decribed earlier (McMichael, 1976). Numerous selection factors were in operation among members of this cohort. Not only did these women meet the requirements described by McMichael (1976) of being healthy enough to be employed, but many of these women held government security clearances. Although difficult to quantify, the additional restrictions involved in obtaining a government clearance should result in an "extra" healthy worker effect. For example, persons with detrimental health practices such as drug and alcohol abuse might not be granted or might hesitate to apply for a clearance. Also significantly low were cancers of the digestive system, cervical cancers, and deaths from circulatory diseases.

Education

Because education was hypothesized to influence the mortality among women in this cohort, the cohort was stratified on the basis of education and SMRs were calculated for the educational subcohorts. Mortality among women with less education than a college degree closely resembled that of the overall cohort. This, of course, was not surprising due to the fact that 79.5% of the cohort fell into this category.

Results for the subcohort of women with a college degree held some surprises. Only the SMR for diseases of the circulatory system was significantly less than 100. SMRs for cancers of the kidney and mental disorders significantly exceeded 100, and the SMR for motor vehicle accidents among college educated Laboratory employees was borderline significant. The finding of elevated rates of deaths due to motor vehicle accidents has been reported previously (Wiggs et al., 1987). Explanations for the elevated SMRs among the college educated subcohort are not readily forthcoming. One possibility is that it is fallacious to compare a college educated cohort with the general population, most of which are not college educated. This may explain why results among the noncollege educated subcohort were not remarkable.

If one considers it acceptable to compare a college educated cohort with the general population, explanations for the high rates of kidney cancer and mental disorders must be sought.

Cigarette smoking has been implicated as a risk factor for kidney cancer (McLaughlin et al., 1984; Morrison and Cole, 1982). Unfortunately, information on smoking was not available for these cases of kidney cancer. Likewise, data on other nonoccupational risk factors associated with the development of kidney cancer (McLaughlin et al., 1984), such as obesity, use of phenacetin analgesics, and meat and tea consumption, were unavailable.

The occupational exposures potentially implicated in the development of kidney cancer include exposure to petroleum, tar and pitch products (McLaughlin et al., 1984). In addition, elevated rates of kidney cancer have been observed among coke oven workers (Redmond et al., 1972), and asbestos insulation workers (Selikoff et al., 1979).

Unfortunately, because industrial hygiene data were not available to permit direct assessment of these potential occupational factors, indirect methods were employed. The three deaths from kidney cancer were employed in jobs not readily indicative of other occupational exposures. Two of these women were employed in secretarial/clerical job titles, while one was employed as a junior scientist/computer. Furthermore, insignificant latency existed between hire date and death date (~19 months) for the woman employed as junior scientist for an occupational exposure encountered at the Laboratory to explain this cancer occurrence.

As a result of this information, it is impossible to explain the high SMR for kidney cancer among this subcohort, but it appears unlikely that a work place exposure was involved in the development of disease among these women.

Regarding the high SMR for the three deaths due to mental disorders, more detailed examination of the cases was required because this is a pooled ICDA category including many diverse causes of death. Two of these deaths were coded as "other and unspecified alcoholism" (ICDA-8 303.9). A careful review of the death certificates revealed one of these deaths was attributed to natural causes and changed based on an autopsy to "acute alcoholism". The other death was recorded as "consistent with accidental death, alcohol intoxication". Because the portion of the certificate designating an accident was labelled "undetermined", this death was assigned a code of 303.9. One must question whether this death should have been coded as an unspecified injury death by the nosologist. Finally, the third certificate was coded 309.9, which was consistent with the cause of death stated on the death certificate, "senile dementia, organic brain disease progressive".

Duration of Employment

Another area examined in the SMR analyses was the question of duration of employment. Occupational studies often employ a work restriction of varying lengths for various reasons (Wilkinson et al., 1987; Gilbert and Marks, 1979; Checkoway et al., 1985). Gilbert and Marks (1979) argued that short term workers should be excluded from these analyses because they generally have less radiation exposure and are less influenced by the healthy worker effect.

The impact of using a six-month work restriction, imposed on this current study due to financial constraints, was assessed by calculating SMRs for the subcohort employed less than six months and the subcohort employed more than six months. Mortality was unremarkable for the 1339 persons employed less than six months. Significantly fewer deaths than expected were observed for all causes, all cancers and all circulatory diseases. No causes were significantly elevated. Mortality among those employed greater than six months closely resembled mortality for the cohort overall. Limiting the radiation exposure and survival analyses to persons employed at least six months should have no noticible impact on the results of these analyses.

Radiation Exposure

Finally, SMRs were used to compare each of the five radiation exposed or monitored subcohorts with expected mortality based on US death rates. The only remarkable finding observed from these comparisons was an excess of suicide mortality among three of these subcohorts compared with expected suicide deaths based on US rates. Table 69 presents the suicide SMRs.

TABLE 69

STANDARDIZED MORTALITY RATIOS FOR SUICIDES AMONG WHITE FEMALES EMPLOYED BY THE LOS ALAMOS NATIONAL LABORATORY

Group	Observed	Expected	SMR	95% CI
All white females (N = 6573)	14	12.55	112	61, 187
All white females employed at least six months (N = 5234)	11	10.24	107	62, 192
Radiation workers (N = 1591)	8	2.91	275	118, 542
Monitored external (N = 1412)	7	2.00	350	140, 720
Cumulative dose at least 1 rem (N = 120)	2	0.22	928	104,3352
Ever bioassayed for plutonium (N = 479)	1	0.79	126	2, 701
Positive plutonium uptake (N = 358)	1	0.51	196	3,1092

The significantly elevated SMRs were observed in the "ever radiation worker" subcohort (SMR = 275, 95% CI = 118, 542), the "ever monitored for external radiation" subcohort (SMR = 350, 95% CI = 140, 720) and the subcohort of women with cumulative radiation exposures in excess of 1 rem (SMR = 928, 95% CI = 104, 3352). No significant excess of suicide was observed among the "plutonium monitored" or "positive plutonium uptake" subcohorts. Only one suicide death was observed among plutonium monitored or body burdened women.

A possible explanation for this phenomenon was that the elevated rates of suicide among radiation and external radiation workers was in fact due to a socioeconomic bias. The only indication of socioeconomic status available for this cohort was education. Education has been related to suicide with women in well educated positions such as physicians (Carlson and Miller, 1981; Steppacher and Mausner, 1974) and chemists (Li, 1969; Gleiser, 1987) demonstrating a higher rate of suicide than women in the general population. Furthermore, the suicide rates among women physicians and women chemists were higher than the rates for men in the same profession (Steppacher and Mausner, 1974; Li, 1969; Gleiser, 1987).

In this cohort, becoming a radiation worker was strongly related to education. This is most likely due to the fact that among women the job titles where radiation exposures are more probable (technician and scientist) are also job titles requiring higher levels of education. Secretarial and clerical job titles, commonly held by women, have little chance of radiation exposure and do not require higher levels of education. Tables 70 through 72 present the relationship between education and becoming a radiation worker, being monitored for external radiation, or being monitored for plutonium. Chi-square tests of the association were performed and odds ratios and their associated 95% confidence intervals were calculated to measure the strength of the association (Rothman and Boice, 1979).

Among radiation workers, 30.2% were at least college graduates compared with 17.9% among the nonradiation workers. The chi-square test of the association was statistically significant and the odds ratios, using "less than high school" as the baseline category, demonstrated a clear linear trend. Similarly, when workers monitored for external radiation were compared with those not monitored, 31.1% of the monitored were college graduates compared with only 18.1% of the nonmonitored. The chi-square test demonstrated a significant association between education and whether or not an individual had been monitored. The odds ratios were also statistically significant and increased with increasing education. Persons with a post graduate degree were three and a half times more likely to be monitored for external radiation than were women who did not finish high school. Finally, 33.0% of the plutonium bioassayed workers held college or advanced degrees compared with 20.4% of the workers never bioassayed for plutonium. This association did not appear to be as strong as for the other radiation categories. The odds ratio for post graduate education was only 1.6. These comparisons were all limited to white women employed at least six months.

TABLE 70

COMPARISON OF EDUCATION AMONG WHITE FEMALE RADIATION AND NONRADIATION WORKERS EMPLOYED AT LEAST SIX MONTHS

	Education					
	Less than High School	High School Graduate	Associates	College Graduate	Post Graduate	Total
Not radiation	769	2105	119	524	130	3647
Radiation	238	807	64	357	123	1589
Total	1007	2912	183	881	253	5236
Odds ratio		1.24	1.74	2.20	3.06	1.77
95% CI		(1.05,1.46)	(1.24,2.43)	(1.81,2.68)	(2.31,4.04)	(1.58,1.98)

$x^2 = 115.98$, 4 d.f., $p < 0.001$

TABLE 71

EDUCATION AMONG WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS: WORKERS MONITORED FOR EXTERNAL RADIATION COMPARED WITH NOT MONITORED FOR EXTERNAL RADIATION

	Education					
	Less than High School	High School Graduate	Associates	College Graduate	Post Graduate	Total
Not monitored	813	2176	124	550	138	3801
Monitored	194	736	59	331	115	1435
Total	1007	2912	183	881	253	5236
Odds Ratio		1.42	1.99	2.52	3.49	2.05
		(1.18,169)	(1.42,2.18)	(2.05,3.10)	(2.63,4.64)	(1.82,2.30)

$x^2 = 129.52$, 4 d.f., $p < 0.001$

TABLE 72

COMPARISON OF EDUCATION FOR PLUTONIUM BIOASSAYED AND NONBIOASSAYED WORKERS AMONG WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS

	Education					
	Less than High School	High School Graduate	Associates	College Graduate	Post Graduate	Total
Never Bioassayed	913	2686	159	747	218	4723
Bioassayed	94	226	23	134	35	512
Total	1007	2912	182	881	253	5235
Odds Ratios		0.82	1.41	1.74	1.56	1.24
95% CI		(0.64,1.05)	(0.87,2.28)	(1.32,2.30)	(1.03,2.36)	(1.05,1.47)

$x^2 = 49.51$, 4 d.f., $p < 0.001$

The relationship between suicide and education was examined among white females employed at least six months. When suicide deaths were compared with members of the cohort deceased from causes other than suicide, a difference in educational attainment was observed for the two groups. Among suicides, 35.7% were college or advanced degree holders, while only 22.9% of the deaths from nonsuicide causes were college or advance degree holders. Although the differences in proportions were substantial, the chi-square test was nonsignificant ($x^2 = 1.24$, 1 d.f., $p = 0.2654$). The odds ratio was 1.87 (95% CI = 0.62, 5.64). Nevertheless, a different pattern of education was observed for suicide and nonsuicide deaths.

The results suggest that female radiation workers, like female physicians and chemists, may experience high rates of suicide. Socioeconomic or psychosocial factors rather than exposure to radiation appear more likely related to this association, although it was not possible to prove this conclusively. This investigation has demonstrated an association between education and both employment as a radiation worker and suicide, although the association between education and suicide was nonsignificant. Extensive mortality follow-up among atomic bomb survivors (Beebe et al., 1978) has not demonstrated increased rates of suicide. In fact, Beebe et al. (1978) reported an inverse relationship between radiation dose and suicide among male atomic bomb survivors. Female atomic bomb survivors in the highest dose category (400+ rem), however, did demonstrate an excess of all injury deaths, but this excess did not appear to be due to suicide (2.0 observed compared with 1.9 expected). Beebe et al. (1978) concluded "analysis disclosed no association with radiation dose that would suggest that the behavior of survivors is so deviant as to influence the likelihood that they may be involved in fatal accidents, suicides, etc.".

An additional check was made to determine whether the suicides observed among these workers were possibly due to an underlying diagnoses of cancer, which could possibly be associated with their radiation exposure. None of the death certificates for any of the women dying from suicide in the cohort contained any mention of cancer. Previous cancer diagnoses, although impossible to rule out completely, appears unlikely to explain the observed pattern of suicides.

Additional studies of suicide among radiation workers, especially females, should be conducted. These future investigations should be expanded to examine both psychosocial factors previously related to suicide rates, such as alcohol abuse (Murphy and Robins, 1967; Kessel and Grossman, 1961), as well as the biological plausibility of an association between radiation exposure and suicide.

Comparison of Mortality Among Radiation Exposed and Unexposed Workers

The goal of these analyses was to determine whether or not women occupationally exposed to radiation experienced higher cancer mortality rates than women not exposed to occupational radiation. The measure employed in these analyses was the rate ratio which directly compared rates among exposed and unexposed members of the cohort. An advantage of this technique was that by comparing rates within the cohort, the bias of the healthy worker effect was minimized or eliminated.

Radiation Compared with Nonradiation Workers

The first comparisons were between radiation and nonradiation workers. None of the rate ratios at any of the seven induction periods considered revealed significant differences between the radiation and nonradiation workers for any cause-specific cancer site. Rate ratios for cancers of the following sites were nonsignificantly elevated: cancers of the pancreas, ovary, and benign neoplasms. Each of these cancer sites was found to be statistically significant in one of the subcohorts (external radiation monitored or plutonium bioassayed) described later.

External Radiation Monitored Workers Compared with Nonmonitored Workers

Ovarian cancer. For comparisons between workers monitored for external radiation and those not monitored for external radiation, an excess of ovarian cancer was observed at two (RR = 3.62, 95% CI = 0.99, 13.20) and five (RR = 4.52, 95% CI = 1.18, 17.28) years induction. These rate ratios were based on four monitored and six nonmonitored cases of ovarian cancer at these induction periods. Table 73 presents the ovarian cancer rate ratios comparing external radiation monitored workers with nonmonitored workers.

These findings are not inconsistent with the findings of the Committee on the Biological Effects of Ionizing Radiations (1980) which stated that "the radiation risk of ovarian-tumor induction is low, but identifiable". Palmer and Spratt (1956) observed 8.0 cases of ovarian cancer compared with 2.6 expected among a group of women treated with

TABLE 73

RATE RATIOS FOR OVARIAN CANCER AMONG WOMEN MONITORED FOR EXTERNAL IONIZING RADIATION EXPOSURE COMPARED WITH WOMEN NOT MONITORED FOR EXTERNAL IONIZING RADIATION EXPOSURE AT SELECTED INDUCTION PERIODS

	Monitored		Not Monitored			
Induction Time (years)	Deaths	Person-Years	Deaths	Person-Years	RR	95% CI
0	4	19554.5	6	85977.4	3.19	0.89,11.46
2	4	16957.5	6	88574.4	3.62	0.99,13.20
5	4	13527.4	6	92004.5	4.52	1.18,17.28
10	3	9312.5	7	96219.4	3.52	0.83,14.97
15	2	5866.1	8	99665.9	2.54	0.49,13.08
20	1	3158.4	9	102373.5	1.68	0.20,14.09
25	0	1311.2	10	104220.7	0.00	0.00,27.77

radiation for benign gynecologic conditions. Among these women, the average interval between irradiation and tumor diagnosis was 10.1 years. This differs some from the pattern of induction times observed in this study, where rate ratios increased through 5 years induction and began to decline starting with 10 years induction (RR = 3.52, 95% CI = 0.83, 14.97).

Doll and Smith (1968) also observed more deaths from ovarian cancer than expected (7 observed compared with 3.75 expected) among women whose ovaries were irradiated with x-rays for the treatment of metropathia haemorrhagica and other gynecological conditions. Only deaths occurring five or more years after radiation were considered.

In a case-control study of ovarian cancer, Annegers et al. (1979) reported a nonsignificant odds ratio of 1.8 (95% CI = 0.9, 3.5) for prior pelvic radiation for the treatment of miscellaneous gynecologic conditions. The authors of this study stated that prior pelvic radiation exposure was not a "significant risk factor" in the development of ovarian cancer.

Among the Hiroshima survivors of the atomic bomb, there is some evidence of an association between radiation exposure and cancers of the ovary (Beebe, 1978). New studies of mortality among atomic bomb survivors report that among Hiroshima survivors "the risk of neoplasm of the ovary is 50% higher among the survivors combined than the non-exposed with the difference being significant" (Kurihara et al., 1981). Tokuoka (1986) reported a statistically significant dose response for ovarian cancer and radiation dose among atomic bomb survivors. Although not statistically significant, a linear relationship with radiaton dose was also observed for benign ovarian tumors. Recently, Preston et al. (1987) reported an increased risk of ovarian cancer among survivors but concluded that "it is premature to conclude that these data provide convincing evidence for a radiation-related excess risk of ovarian cancers".

Finally, in studies of female nuclear workers some evidence suggesting increased ovarian cancer has been observed. For example, Beral et al. (1985) observed an SMR of 183 for the combined category of cervical/uterine/ovarian cancer among female radiation workers employed by the United Kingdom Atomic Energy Authority. When examined as separate categories, SMRs for cervical, ovarian, and uterine cancers were each elevated; however, only the SMR for uterine cancer was statistically significant.

Among female Hanford workers (Gilbert et al., submitted), a borderline significant dose response was observed for radiation and the collective category of all female genital cancers. This category included cervical, uterine, and ovarian tumors.

A careful review of the Los Alamos ovarian cancer cases revealed that only one of the four monitored cases had a cumulative radiation exposure of at least 1 rem. This was a physicist employed by the Laboratory from 1943 until her death in 1972. This woman had been monitored for radiation exposure since 1947 and had a cumulative radiation dose in excess of 16 rems. Her cumulative exposure exceeded 10 rems in 1952; therefore, a long potential latency for the development of cancer was present. This woman was never bioassayed for plutonium.

The rate ratios comparing ovarian cancer among women with cumulative radiation of at least 1 rem with women who were monitored, but had cumulative exposures of less than 1 rem, were nonsignificantly elevated. Table 74 presents a summary of these rate ratios over six induction periods. It is interesting that these rate ratios steadily increased with increasing induction time to a rate ratio of 5.66 (95% CI = 0.51, 62.73) at 20 years induction. However, because ratios are based on only one exposed case and a very limited number of person years, it is very difficult to assess the meaning of these results.

None of the 10 Los Alamos cases of ovarian cancer were monitored for plutonium exposure from 1945 through 1981. One of the cases of ovarian cancer among the Hanford population (Gilbert et al., submitted) had a confirmed plutonium body burden (3.2 nCi) occurring 22 years prior to death. This case also had a rather large exposure to external radiation (between 5 and 15 rems). Gilbert et al. (submitted) felt that there was no reason to suspect that this ovarian cancer was related to the plutonium deposition.

Finally, other risk factors for the development of ovarian cancer must be considered. Occupational risk factors implicated in the development of ovarian cancer include asbestos and talc (Weiss, 1982). A discussion with a Los Alamos industrial hygienist confirmed that asbestos has been used in Laboratory operations over the years. No operations using significant quantities of talc are known to have occurred (Talley, 1987). Again, because detailed industrial hygiene records are unavailable for individuals, a review of job titles was the only available way to assess potential for occupational exposure.

TABLE 74

RATE RATIOS FOR OVARIAN CANCER AMONG WOMEN MONITORED FOR EXTERNAL RADIATION COMPARING THOSE WOMEN WITH CUMULATIVE RADIATION EXPOSURES OF $\geq$1 REM (EXPOSED) WITH WOMEN WITH CUMULATIVE RADIATION EXPOSURE OF <1 REM (UNEXPOSED)

Induction Time (years)	Exposed Deaths	Exposed Person-Years	Unexposed Deaths	Unexposed Person-Years	RR	95% CI
0	1	2056.2	3	17498.3	1.82	0.19, 17.51
2	1	1832.3	3	17722.2	1.88	0.20, 18.17
5	1	1551.8	3	18006.1	2.13	0.22, 20.60
10	1	1147.7	3	18406.8	2.69	0.27, 27.06
15	1	820.4	3	18753.6	3.38	0.31, 36.42
20	1	504.3	3	19072.5	5.66	0.51, 62.73

Eight of the 10 cases held secretarial/clerical positions, 1 was a school teacher and 1 (as mentioned earlier) was a physicist. Based on the job titles among the cases, there is no reason to suspect that any of the cases, except perhaps the physicist, might have occupational exposure to asbestos. Further review of this woman's (the physicist) occupational record, although not conclusive, revealed no evidence of asbestos exposure.

Other risk factors, such as nulliparity or low parity, may be more important among this cohort than exposure to occupational carcinogens. Previous studies have demonstrated an inverse relationship for ovarian cancer and parity (Beral et al., 1978) and an inverse relationship for ovarian cancer with the number of pregnancies (Joly et al., 1974; Casagrande et al., 1979). In fact, in the study by Joly et al. (1974) the maximum relative risk was observed for the category "never pregnant". Joly et al. (1974) also found that age at first pregnancy was associated with ovarian cancer with women becoming pregnant at older ages experiencing a higher risk of ovarian cancer.

The study of Casagrande et al. (1979) noted that pregnancy suppressed ovulation; therefore, they examined factors related to anovulation including pregnancy and use of oral contraceptives. They (Casagrande et al., 1979) found that "the risk of ovarian cancer is clearly decreased directly by factors which suppress ovulation".

Positive associations between ovarian cancer and increasing education (Joly et al., 1974) and increasing socioeconomic status (Graham et al., 1960) have been reported. In the investigation of Los Alamos women, the only available indicator of socioecomomic status was education. Because education has been previously associated with the risk of ovarian cancer (Joly et al., 1974) and because education has been associated with the chances of being monitored for external radiation among Los Alamos female employees, education was considered a potential confounding factor in the relationship between developing ovarian cancer and being monitored for external radiation observed in this cohort.

In order to examine this, the relationship between ovarian cancer and education (Table 75) among the Los Alamos cohort was investigated. A test of the association revealed a borderline significant result (x^2 = 8.551, 4 d.f., p = 0.07), but the directions of the differences were confusing. For example, 16.7% of the ovarian cancers held post graduate degrees while only 3.5% of the deaths from other causes held graduate degrees. The odds ratio for graduate education was borderline significant at 5.48 (95% CI = 1.00, 29.87). On the other hand, a higher proportion of the ovarian cancers had no college education (83.3%) than the deaths from other causes (72.9%). Education may contribute but does not appear to fully explain the results observed for ovarian cancer in this subcohort.

As a result, the findings of increased ovarian cancer among women in the external monitored subcohort cannot be adequately explained. Radiation exposures for all but one of the monitored women were trivial and unlikely to contribute to the development of cancers. Education alone may account for some of the effect observed, although the effect is probably a result of a number of socioeconomic and lifestyle factors which this study was unable to evaluate.

TABLE 75

COMPARISON OF EDUCATION FOR OVARIAN CANCER DEATHS AND DEATHS FROM OTHER CAUSES AMONG WHITE FEMALES EMPLOYED AT LEAST SIX MONTHS

	Education					
	Less than High School	High School Graduate	Associates	College Graduate	Post Graduate	Total
Ovarian Cancer	3	7	0	0	2	12
Other Causes	115	173	14	79	14	395
Total	118	180	14	79	16	407
Odds Ratios		1.55	---	---	5.48	2.40
95% CI		(0.40,6.07)			(1.00,29.87)	(0.71,8.16)

$x^2 = 8.55$, 4 d.f., $p = 0.0734$

All causes. At 10 and 15 years induction, rate ratios for the collective category of "all causes" were significantly elevated. Interpretation of findings of generally increased mortality among a group of workers is difficult unless one hypothesizes general life shortening as the result of the exposure of interest.

Some have discussed such an effect associated with radiation exposure. It has been hypothesized that radiation exposed animals die at earlier ages than nonexposed animals. Studies in nonhuman animals have suggested that this is true. Furthermore, these studies indicate that life shortening is increased with larger exposures. Chronic exposures, such as those received by members of the Los Alamos cohort, result in less life shortening compared with an acute exposure for the same dose, accounting for approximately 1% per 100 rads (Casarett, 1968). This life shortening has been attributed to an increase in deaths due to radiation induced cancers, an increase in the natural aging process, and to an early onset of both neoplastic and nonneoplastic diseases (Casarett, 1968; Walburg, 1975; International Commission on Radiation Protection, 1969).

This theory is controversial and not well supported by the studies of man. Seltzer and Sartwell (1958) concluded that they observed a life shortening effect based on the large number of deaths due to cardiovascular diseases among the cohort of American radiologists. Their conclusions have been disputed (Walburg, 1975) and have not been supported by the studies among British radiologists (Court Brown and Doll, 1958). Court Brown and Doll (1965) stated that there was "no evidence that occupational exposure to ionizing radiations has caused a detectable nonspecific shortening of the expectation of life". Later studies among American radiologists, however, again concluded that a life shortening effect was observed (Matanoski et al., 1975a; Matanoski et al., 1975b).

Jablon and Kato (1972) did not find evidence to support a theory of generalized life shortening among the atomic bomb survivors. Similarly, Beebe et al. (1978) found no evidence of nonspecific life shortening or accelerated aging among atomic bomb survivors. Beebe et al. (1978) concluded that "the evidence from the studies of A-bomb survivors is that the late mortality effects of large, single doses of ionizing radiation are focal, and largely confined to cancer". They concluded that the differences between the atomic bomb survivors and the radiologists must be due to confounding factors in the radiologist studies or the differences between chronic and acute doses.

A comparison of survival distributions for external monitored and nonmonitored workers found no difference in survival time between these groups. This finding does not support the hypothesis of generalized life shortening among the monitored group.

A review of the distribution of cancer deaths did not point out any cancer-specific cause that could explain this excess of "all causes" mortality among the radiation monitored. Rate ratios for cancers of the pancreas, ovary, and benign neoplasms were elevated, but only the rate ratio for cancers of the ovary was based on more than one exposed case. These observations were true for both 10 and 15 years induction and were unlikely to explain the elevated "all causes" rate ratios based on 56 and 44 total exposed deaths at 10 and 15 years, respectively.

Because cancer-specific causes did not appear to account for the excess of "all causes" mortality, noncancer causes were examined. As noted earlier, the SMR for suicide among the external radiation monitored subcohort was elevated (SMR = 350, 95% CI = 140, 720); therefore, an analysis was conducted to determine whether the excess of suicides noted earlier accounted for the excess rate ratios for "all causes" of death among this group. Analyses were repeated excluding deaths due to suicide from both the monitored and nonmonitored subcohorts. Although still greater than 1.00, rate ratios for "all causes" were no longer statistically significant for 10 years (RR = 119, 95% CI = 0.87, 1.63) and 15 years (RR = 1.24, 95% CI = 0.88, 1.75) induction.

Likewise, rate ratios comparing suicide among monitored and nonmonitored women were computed. These rate ratios were significantly elevated at both 10 (RR = 11.55, 95% CI = 3.25, 41.06) and 15 (RR = 6.67, 95% CI = 1.66, 26.85) years induction; therefore, it appears that the significantly elevated rate ratios for all causes of death for external radiation monitored compared with nonmonitored workers can be explained at least in part by the high rates of suicide among the workers monitored for external radiation.

Pancreatic cancer. At 25 years induction, an excess of pancreatic cancer was observed for external monitored workers compared with workers never monitored for external radiation. Table 76 summarizes the rate ratio for pancreatic cancers at the various

TABLE 76

RATE RATIOS FOR PANCREATIC CANCER AMONG WOMEN MONITORED FOR EXPOSURE TO EXTERNAL RADIATION AND THOSE NOT MONITORED FOR EXPOSURE TO EXTERNAL RADIATION

	Monitored		Not Monitored			
Induction Time (years)	Deaths	Person-Years	Deaths	Person-Years	RR	(95% CI
0	1	19554.5	1	85977.4	3.71	0.23, 59.39
2	1	16957.5	1	88574.4	3.87	0.24, 61.87
5	1	13527.4	1	92004.5	4.13	0.26, 66.13
10	1	9312.5	1	96219.4	4.78	0.30, 76.51
15	1	5866.1	1	99665.9	6.43	0.40,104.08
20	1	3158.4	1	102373.5	10.61	0.65,174.45
25	1	1311.2	1	104220.7	36.59	1.68,795.25

induction times. The pancreatic rate ratios increased steadily with increasing induction time. The observed rate ratios are based on only one case among the monitored and one case among the nonmonitored. At 25 years induction, there were only 1311.2 person-years in the monitored subcohort. The monitored case had cumulative radiation exposures of less than 1 rem.

There has been considerable discussion of pancreatic cancer among radiation workers and radiation exposed groups in recent years. In 1979, Gilbert and Marks (1979) reported a significant dose response for radiation exposure and cancer of the pancreas. In the highest exposure category examined (15+ rems), three deaths from pancreatic cancer were observed compared with one death expected.

Subsequently, however, this finding of excess pancreatic cancer among Hanford workers has been refuted. Tolley et al. (1983) reported that the significant dose response for cancer of the pancreas was no longer observable in the Hanford cohort. Furthermore, review of the pancreatic cancers revealed that one of the deaths in the high dose category was incorrectly recorded as a pancreatic cancer death (Gilbert and Marks, 1980).

Other studies of radiation exposure and pancreatic cancer have also produced contradictory results. For example, studies of atomic bomb survivors have estimated the relative risk of pancreatic cancer at 1.00 (Kato, 1986; Preston et al., 1987). A study of British radiologists, on the other hand, reported evidence of excess deaths from pancreatic cancer (6 observed compared with 1.4 expected) among radiologists joining a professional society before 1921 (when new radiation protection recommendations were proposed).

A close review of the two Los Alamos cases of pancreatic cancer, one monitored for external ionizing radiation and the other not monitored, revealed no evidence of significant exposure to substances other than radiation. The nonmonitored woman's personnel record stated that she worked outside the technical area. The only exposure other than radiation noted for the monitored woman was occasional exposure to corrosive substances used in decontaminating her equipment. This woman's cumulative radiation exposure was 690 mrems; therefore, it is highly unlikely that her radiation exposure contributed to the development of her pancreatic cancer.

Workers With Cumulative Radiation Doses of at Least 1 Rem Compared With Workers With Less Than 1 Rem

All causes. As observed earlier when external radiation monitored workers were compared with nonmonitored workers, elevated rate ratios were observed for all causes of death for workers exposed to at least 1 rem of cumulative radiation exposure compared with workers exposed to less than 1 rem of cumulative radiation exposure. These elevated rate ratios (Table 77) were statistically significant at 15 and 20 years induction. The rate ratio at 10 years was borderline significant. As with the earlier comparison, suicide was suspected as a possible explanation for these findings. Not only was the suicide SMR (SMR = 928, 95% CI = 104, 3352) significantly elevated for the subcohort with cumulative radiation doses in excess of 1 rem, but also suicide accounted for 2 out of 12 total deaths (16.7%) at 0 years induction and 2 out of 9 total deaths (22.2%) at 15 years induction.

TABLE 77

RATE RATIOS FOR ALL CAUSES AMONG WOMEN WITH CUMULATIVE RADIATION DOSES OF >1 REM COMPARED WITH THOSE WITH CUMULATIVE RADIATION DOSES OF <1 REM

Induction Time (years)	At Least One Rem		Less Than One Rem		RR	95% CI
	Deaths	Person-Years	Deaths	Person-Years		
0	12	2056.2	53	17498.3	1.81	0.95,3.45
2	11	1832.3	54	17722.2	1.73	0.89,3.37
5	10	1551.8	55	18006.1	1.69	0.85,3.38
10	10	1147.7	55	18406.8	1.98	0.99,3.97
15	9	820.4	56	18753.6	2.14	1.03,4.45
20	8	504.3	57	19072.5	2.74	1.26,5.95

Stratified analyses were repeated eliminating suicides from both the subcohort with cumulative radiation doses of at least 1 rem and the subcohort with radiation doses less than 1 rem. The new all causes rate ratios are presented in Table 78.

When the suicide deaths were removed from the "all causes" analyses, only the rate ratio for 20 years induction remained significant (RR = 2.47, 95% CI = 1.08, 5.63). This might be explained by examining the rate ratios for suicide in workers with greater than 1 rem compared with those with less than 1 rem. All of these suicide rate ratios (Table 79) are significantly elevated except for the ratio for 20 years induction (RR = 8.93, 95% CI = 0.82, 96.97).

At 20 years induction, 5 of the deaths contributing to the "all causes" rate ratio were from diseases of the circulatory system. Only two of the deaths were the result of cancer, one breast cancer and one ovarian cancer.

Ever Bioassayed for Plutonium Compared With Never Bioassayed for Plutonium

The only statistically significant result observed for bioassayed compared with nonbioassayed workers was the rate ratio for benign neoplasms at 15 years induction. Table 80 summarizes the rate ratios for benign neoplasms among the bioassayed and nonbioassayed workers. Because "benign neoplasms" includes a number of different tumors, the death certificates were examined closely. The bioassayed death was attributed to a benign brain tumor, while the nonbioassayed death was due to a uterine fibroma; therefore, comparing these diverse diseases may be questionable. The significance of the benign brain

TABLE 78

RATE RATIOS FOR ALL CAUSES EXCLUDING SUICIDES AMONG WOMEN WITH CUMULATIVE RADIATION DOSES OF ≥1 REM COMPARED WITH THOSE WITH CUMULATIVE RADIATION DOSES OF <1 REM

	At Least One Rem		Less Than One Rem			
Induction Time (years)	Deaths	Person-Years	Deaths	Person-Years	RR	95% CI
0	10	2056.2	48	17498.3	1.56	0.78,3.14
2	9	1832.3	49	17722.2	1.47	0.71,3.02
5	8	1551.8	50	18006.1	1.40	0.65,2.99
10	8	1147.7	50	18406.8	1.62	0.75,3.48
15	7	820.4	51	18753.6	1.66	1.74,3.74
20	7	504.3	51	19072.5	2.47	1.08,5.63

TABLE 79

RATE RATIOS COMPARING SUICIDE AMONG WOMEN WITH CUMULATIVE RADIATION DOSES OF ≥1 REM WITH THOSE WITH CUMULATIVE RADIATION DOSES OF <1 REM: 1944-1981

	At Least One Rem		Less Than One Rem			
Induction Time (years)	Deaths	Person-Years	Deaths	Person-Years	RR	95% CI
0	2	2056.2	5	17498.3	6.32	1.12, 35.85
2	2	1832.3	5	17722.2	7.00	1.19, 41.27
5	2	1551.8	5	18006.1	7.50	1.28, 44.04
10	2	1147.7	5	18406.8	11.11	1.83, 67.60
15	2	820.4	5	18753.6	19.48	2.87,132.31
20	1	504.3	6	19072.5	8.93	0.82, 96.97

TABLE 80

RATE RATIOS FOR BENIGN NEOPLASMS AMONG WOMEN BIOASSAYED FOR PLUTONIUM COMPARED WITH WOMEN NOT BIOASSAYED FOR PLUTONIUM AT SELECTED INDUCTION PERIODS

Induction Time (years)	Bioassayed Deaths	Bioassayed Person-Years	Never Bioassayed Deaths	Never Bioassayed Person-Years	RR	95% CI
0	1	7965.7	1	95253.8	9.76	0.61,156.13
2	1	7086.2	1	96133.2	9.94	0.62,159.02
5	1	5868.2	1	97351.3	10.51	0.66,168.08
10	1	4394.5	1	98825.0	12.71	0.80,203.27
15	1	3117.4	1	100102.1	17.36	1.09,277.61
20	0	2001.2	2	101218.3	0.00	0.00,175.63
25	0	1083.7	2	102135.8	0.00	0.00,327.45

tumor is that an excess of these tumors has been observed among another cohort of nuclear workers. Among workers at the Rocky Flats Plant, a significantly elevated SMR was reported for benign tumors, all of which were intracranial tumors (Wilkinson et al., 1983). A subsequent case control study examined brain tumors among this cohort and found no association with external radiation exposure or plutonium body burden (Reyes et al., 1984). The most recent follow-up among members of the Rocky Flats cohort (Wilkinson et al., 1987) found that the SMR for benign tumors was still significantly elevated and still due entirely to intracranial tumors. No association was observed between benign brain tumors and plutonium body burden in this investigation. Some evidence, although nonsignificant, was observed that would support an association between these tumors and external ionizing radiation exposure.

Positive Plutonium Bioassay Compared With No Positive Plutonium Bioassay

A total of 27 deaths occurred among bioassayed women (n=479), with 6 deaths due to cancer. All but 4 of the bioassayed deaths and 358 of the bioassayed women had at least one plutonium urinalysis result indicating some positive uptake. Very few, however, demonstrated measureable body burdens. For this reason, it is very difficult to interpret the results of the analyses comparing positive uptake versus no positive uptake.

None of the rate ratios for the comparisons between positive uptake and no positive uptake people were statistically significant; however, at 5 and 15 years induction the all causes rate ratios were borderline. No obvious explanation is available for these results, but the problems of the statistical variability of results based on such small numbers cannot be ruled out. Detailed interpretation of these findings is not possible at this time. Perhaps with more follow-up, or when the results for Los Alamos males are available, these findings will be more interpretable.

Survival Analyses

The results of the survival analyses are difficult to interpret because they are based primarily on censored observations (~95%). Complete survival experience was unknown for most of the cohort because most were still alive at the EOS. As a result, the only meaningful findings were the comparisons of survival between the radiation subgroups. No significant differences in survival were observed for radiation workers compared with nonradiation workers, for workers monitored for external radiation compared with workers not monitored, or for plutonium bioassayed workers compared with workers never bioassayed.

In the future, the usefulness of survival analyses will improve as a higher proportion of the cohort is deceased. Furthermore, it may be prudent to limit future survival analyses of this type to older subcohorts, for example workers hired during the 1940's, for whom a smaller proportion of the observations will be censored.

Strengths and Limitations

As with any investigation, this study had strengths and limitations. The limitations included the small number of radiation exposed workers and the generally low levels of their cumulative exposures. This limited the analyses that were possible. Ideally, analyses of external radiation would have focussed on the analyses of $\geq$1 rem compared with <1 rem. Analyses would have also included a dose-response approach. The data, however, precluded this and required cruder measures of exposure, such as comparisons between monitored and nonmonitored workers. The comparisons of radiation workers and nonradiation workers were necessitated by the absence of film badge data for the earliest years of operation at Los Alamos. Similarly, with the plutonium analyses the preferred approach would have compared body burdened individuals with individuals with no body burden and would have included dose-response analyses. Unfortunately, analyses had to be limited to the comparisons of monitored/nonmonitored and positive urinalyses/no positive urinalyses.

Another limitation was the limited availability of industrial hygiene records for use in ascertaining exposures to chemical and other potential hazards in the work place. As with any study relying on historical data, this study did not have access to information on a number of potential confounders, such as smoking and reproductive histories. Finally, although good for the cohort overall, the small percentage of deceased individuals severely limited the appropriateness and use of survival techniques.

The strengths of the study were that vital status was successfully ascertained (93%) for a large cohort of female workers employed over nearly a 40-year period. Average follow-up time exceeded 20 years. Cause of death was obtained for over 95% of those thought to be deceased.

Excellent personnel radiation dosimetry was available for individual cohort members beginning in 1944-1945. These data allowed investigators to not only look at the cumulative exposures, but allowed the examination of the time patterns associated with the radiation exposure. It was possible to include induction time in the analyses and to consider whether the exposure plausibly preceded the onset of disease. Furthermore, these dosimetry records allowed assignment of an exposure history to an individual rather than a work area or job title as is often done in occupational studies.

CHAPTER VII

SUMMARY

A historical cohort analyses of 6790 women employed by the Los Alamos Laboratory has been conducted. This epidemiologic investigation focussed on two questions. First, it sought to determine whether mortality among members of this cohort differed significantly from mortality among females in the United States population. Second, it sought to determine whether workers exposed to radiation in their jobs were at an increased risk of dying from cancer compared with workers who were never exposed to radiation at work.

To address the first question, standardized mortality analyses, using US death rates to generate expected values, were conducted. In general, observed mortality was less than expected, and no cause significantly exceeded expectation. The standardized mortality ratios (SMRs) were 76 and 78 for all causes and all cancers, respectively. Suicide SMRs calculated to compare mortality rates among the subcohort of radiation workers with expected values, were significantly elevated.

To address the second question, stratified analyses directly comparing mortality rates for radiation exposed and nonexposed members of the cohort were conducted. Rate ratios for cancers of the ovary and pancreas were found to be significantly elevated. Previous epidemiologic evidence indicates that these cancers may be associated with radiation exposure, although in this cohort radiation exposure appears unlikely to explain these findings. Other cancers, previously reported to be associated with radiation exposure, like leukemias, were not found to be elevated among this cohort.

An elevated risk for deaths due to all causes among radiation workers was explained by an elevated risk of suicide. This finding, while thought unlikely associated with any biologic effects of exposure, has not yet been explained by other factors. Additional work needs to be conducted to understand this finding.

BIBLIOGRAPHY

John F. Acquavella, Gregg S. Wilkinson, Gary L. Tietjen, Charles R. Key, and George L. Voelz, "Malignant Melanoma Incidence at the Los Alamos National Laboratory," Lancet i: 883-884 (April 17, 1982).

John F. Acquavella, G. S. Wilkinson, L. D. Wiggs, G. L. Tietjen, and C. R. Key, "An Evaluation of Cancer Incidence Among Employees at the Los Alamos National Laboratory," in Epidemiology Applied to Health Physics, Proceedings of the Health Physics Society, January 9-13, 1983, CONF-830101 (National Technical Information Service, Springfield, Virginia, 1983a), pp. 338-345.

J. F. Acquavella, G. S. Wilkinson, G. L. Tietjen, C. R. Key, J. H. Stebbings, and G. L. Voelz, "A Melanoma Case-Control Study at the Los Alamos National Laboratory," Health Physics 45: 587-592 (1983b).

E. E. Adams and A. M. Brues, "Breast Cancer in Female Radium Dial Workers First Employed Before 1930," Journal of Occupational Medicine 22: 583-587 (1980).

John F. Annegers, H. Strom, David G. Decker, Malcolm B. Dockerty, and W. Michael O'Fallon, "Ovarian Cancer, Incidence and Case-Control Study," Cancer 43: 723-729 (1979).

V. E. Archer, J. K. Wagoner, and F. E. Lundin, Cancer Mortality Among Uranium Mill Workers," Journal of Occupational Medicine 15: 11-14 (1973).

Donald F. Austin, Peggy J. Reynolds, Mildred A. Snyder, Max W. Biggs, and Harrison A. Stubbs, "Malignant Melanoma Among Employees of Lawrence Livermore National Laboratory," Lancet ii: 712-716 (1981).

Donald F. Austin and Peggy Reynolds, "A Case-Control Study of Malignant Melanoma Among Employees of Lawrence Livermore National Laboratory," Report #3, July 3, 1984.

K. F. Baverstock, D. Papworth, and J. Vennart, "Risks of Radiation at Low Dose Rates," Lancet i: 430-433 (1981).

K. F. Baverstock and J. Vennart, "A Note on Radium Body Content and Breast Cancer in U.K. Radium Luminisers," Health Physics 44 (Supplement 1): 575-577-(1983).

G. W. Beebe, H. Kato, and C. E. Land, "Studies of the Mortality of A-Bomb Survivors, 6. Mortality and Radiation Dose, 1950-1974," Radiation Research 75: 138-201 (1978).

Valerie Beral, Patricia Fraser, and Clair Chilvers, "Does Pregnancy Protect Against Ovarian Cancer?," Lancet i: 1083-1086 (1978).

Valerie Beral, Hazel Inskip, Patricia Fraser, Margaret Booth, Derek Coleman, and Geoffrey Rose, "Mortality of Employees of the United Kingdom Atomic Energy Authority, 1946-1979," British Medical Journal 291: 440-447 (1985).

BMDP (Biomedical Data Processing, Inc.), BMDP Statistical Software, ed. W. J. Dixon (University of California Press, Berkeley, CA, 1985).

J. D. Boice and R. R. Monson, "Breast Cancer in Women After Repeated Fluoroscopic Examinations of the Chest," Journal of the National Cancer Institute 59: 823-832 (1977).

Norman Breslow, "A Generalized Kruskal-Wallis Test for Comparing K Samples Subject to Unequal Patterns or Censorship," Biometrika 57: 579-594 (1970).

Bureau of the Census, US Department of Commerce, "1980 Census of Population and Housing, Summary Characteristics for Govermental Units and Standard Metropolitan Statistical Areas: New Mexico," PHC80-3-33 (US Government Printing Office, Washington DC, May 1987a).

Bureau of Census, US Department of Commerce, "1980 Census of Population, General Population Characteristics: New Mexico," PC80-1-B33 (US Government Printing Office, Washington DC, May 1982b).

Gabrielle A. Carlson and Diana C. Miller, "Suicide, Affective Disorder, and Women Physicians," American Journal of Psychiatry 138: 1330-1335 (1981).

J. T. Casagrande, E. W. Louie, M. C. Pike, S. Roy, R. K. Ross, and B. B. Henderson, "Incessant Ovulation and Ovarian Cancer," Lancet ii: 170-172 (1979).

Alison P. Casarett, Radiation Biology (Prentice-Hall, Inc., Englewood Cliffs, N. J., 1968) pp. 32-41, 268-273.

H. Checkoway, R. M. Matthew, C. M. Shy, J. E. Watson, Jr., W. G. Tankersley, S. H. Wolf, J. C. Smith, and S. A. Fry, "Radiation, Work Experience and Cause-Specific Mortality Among Workers at an Energy Research Laboratory," British Journal of Industrial Medicine 42: 525-533 (1985).

A. Chovil, "The Epidemiology of Primary Lung Cancer in Uranium Miners in Ontario," Journal of Occupational Medicine 23: 417-421 (1981).

Committee on the Biological Effects of Ionizing Radiations, The Effects on Populations of Exposure to Low Levels of Ionizing Radiation: 1980 (National Academy Press, Washington, D. C., 1980), p. 136, 406-409.

W. M. Court Brown and R. Doll, "Mortality from Cancer and Other Causes After Radiotherapy for Ankylosing Spondylitis," British Medical Journal 2: 1327-1332 (1965).

J. da Silva Horta, L. Cayolla da Motta, and M. H. Tavares, "Thorium Dioxide Effects in Man, Epidemiological, Clinical, and Pathological Studies (Experience in Portugal)," Environmental Research 8: 131-159 (1974).

J. da Silva Horta, M. E. da Silva Horta, L. Cayolla da Motta, and M. H. Tavares, "Malignancies in Portuguese Thorotrast Patients," Health Physics 35: 137-151 (1978).

Department of Energy, Final Environmental Impact Statement, Los Alamos Scientific Laboratory Site, DOE/EIS-0018 (National Technical Information Service, Springfield, Virginia, 1979), pp. 2-1, 2-2, 2-3.

Richard Doll and P. G. Smith, "The Long-Term Effects of X Irradiation in Patients Treated for Metropathia Haemorrhagica," British Journal of Radiology 41: 362-368 (1968).

M. Faber, "Malignancies in Danish Thorotrast Patients," Health Physics 35: 153-158 (1978).

Ethel S. Gilbert and Sidney Marks, "An Analysis of the Mortality of Workers in a Nuclear Facility," Radiation Research 79: 122-148 (1979).

E. S. Gilbert and S. Marks, "An Updated Analysis of Mortality of Workers in a Nuclear Facility," Radiation Research 83: 740-741 (1980).

Ethel S. Gilbert, Gerald R. Petersen, and Jeffrey A. Buchanan, "Mortality of Workers at the Hanford Site: 1945-1981," submitted to Health Physics (April 1987).

Molly Gleiser, "Suicide Among Women Chemists," Nature 328: 10 (1987).

Saxon Graham, Morton Levin, and Abraham Lilienfeld, "The Socioeconomic Distribution of Cancer of Various Sites in Buffalo, N. Y., 1948-1952," Cancer 13: 180-191 (1960).

L. H. Hempelmann, W. H. Langham, C. R. Richmond, and G. L. Voelz, "Manhattan Project Plutonium Workers: A Twenty-Seven Year Follow-Up Study of Selected Cases," Health Physics 25: 461-479 (1973).

L. H. Hempelmann, University of Rochester School of Medicine (retired), personal communication (February 11, 1987).

International Commission on Radiation Protection, "Report of Committee II on Permissible Dose for Internal Radiation (1959)," Health Physics 3: 1-40 (1959).

International Commission on Radiation Protection, "Report of the Task Group to Consider the Relative Radiosensitivities of Different Tissues," in Radio-Sensitivity and Spatial Distribution of Dose, Publication 14 (Pergamon Press, New York, 1969) pp. 17-19.

S. Jablon and H. Kato, "Studies of the Mortality of A-Bomb Survivors. 5. Radiation Dose and Mortality, 1950-1970," Radiation Research 50: 649-698 (1972).

Daniel J. Joly, Abraham M. Lilienfeld, Earl L. Diamond, and Irwin J. Bross, "An Epidemiologic Study of the Relationship of Reproductive Experience to Cancer of the Ovary," American Journal of Epidemiology 99: 190-209 (1974).

Hiro Kato, "Cancer Mortality" in Cancer in Atomic Bomb Survivors eds. Itsuzo Shigematsu and Abraham Kagan (Japan Scientific Societies Press, Tokyo) Plenum Press, New York, 1986) pp. 53-74.

Neil Kessel and Gerald Grossman, "Suicide in Alcoholics," British Medical Journal 2: 1671-1672 (1961).

Kenneth J. Kopecky, "Health Effects of Ionizing Radiation Among Japanese Atomic Bomb Survivors," presented at the Twentieth Annual Meeting of the Society for Epidemiologic Research, Amherst, Massachusetts, June 16-19, 1987.

James W. Kunetka, City of Fire: Los Alamos and the Atomic Age, 1943-1945 (revised edition) (University of New Mexico Press, Albuquerque, NM, 1979), pp. 3-9, 51-52, 123-124.

M. Kurihara, M. Munaka, N. Hayakawa, H. Yamamoto, H. Ueoka, and M. Ohtaki, "Mortality Statistics Among Atomic Bomb Survivors in Hiroshima Prefecture, 1968-1972," Journal Radiation Research 22: 456-471 (1981).

James N. P. Lawrence, "A History of PUQFUA: Plutonium Body Burden (Q) from Urine Assays," Los Alamos Scientific Laboratory report LA-7403-H (October 1978).

H. S. Martland, P. Conlon, and J. P. Knef, "Some Unrecognized Dangers in the Use and Handling of Radioactive Substance," Journal of the American Medical Association 85: 1769-1776 (1925).

H. S. Martland, "Occupational Poisoning in Manufacture of Luminous Watch Dials," Journal of the American Medical Association 92: 466-473 (1929).

Fredrick P. Li, "Suicide Among Chemists," Archives of Environmental Health 19: 518-520 (1969).

George Littlejohn, Los Alamos National Laboratory (retired), personal communication (February 2, 1987).

Los Alamos National Laboratory, Los Alamos Log Book S-3633 (September 9, 1983), p. 51.

G. M. Matanoski, R. Seltser, P. E. Sartwell, E. L. Diamond, and E. A. Elliott, "The Current Mortality Rates of Radiologists and Other Physician Specialists: Deaths From All Causes and From Cancer," American Journal of Epidemiology 101: 188-198 (1975a).

G. M. Matanoski, R. Seltser, P. E. Sartwell, E. L. Diamond, and Elizabeth A. Elliott, "The Current Mortality Rates of Radiologists and Other Physician Specialists: Specific Causes of Death," American Journal of Epidemiology 101: 199-210 (1975b).

C. W. Mays and H. Speiss, "Bone Sarcomas in Patients Given Radium-224," in Radiation Carcinogenesis: Epidemiology and Biological Significance, J. D. Boice and J. F. Fraumeni, Jr., Eds. (Raven Press, New York, 1984) pp. 241-252.

D. H. McGregor, C. E. Land, K. Choi, S. Tokuoka, P. I. Liu, T. Wakabayashi, and G. W. Beebe, "Breast Cancer Incidence Among Atomic Bomb Survivors, Hiroshima and Nagasaki, 1950-69," Journal of the National Cancer Institute 59: 799-811 (1977).

Joseph K. McLaughlin, Jack S. Mandel, William J. Blot, Leonard M. Schuman, Eric S. Mehl, and Joseph F. Fraumeni, "A Population-Based Case-Control Study of Renal Cell Carcinoma," Journal of the National Cancer Institute 72: 275-284 (1984).

A. J. McMichael, "Standardized Mortality Ratios and the "Healthy Worker-Effect": Scratching Beneath the Surface," Journal of Occupational Medicine 18: 165-168 (1976).

Richard R. Monson, "Analyses of Relative Survival and Proportional Mortality," Computers and Biomedical Research 7: 325-332 (1974).

M. V. Morgan and J. M. Samet, "Radon Daughter Exposures of New Mexico U Miners, 1967-1982," Health Physics 50: 656-662 (1986).

Alan S. Morrison and Phillip Cole, "Urinary Tract," in Cancer Epidemiology and Prevention eds. David Schottenfeld and Joseph F. Fraumeni (W. B. Saunders, Co., Philadelphia, 1982), pp. 925-937.

George E. Murphy and Eli Robins, "Social Factors in Suicide," Journal of the American Medical Association 199: 303-308 (1967).

I. Najarian and T. Colton, "Mortality From Leukemia and Cancer in Shipyard Nuclear Workers," Lancet i: 1018-1020 (1978).

National Center for Health Statistics, Public Health Service, US Department of Health, Education, and Welfare, Eighth Revision International Classification of Diseases, Adapted for use in the United States, (Volumes 1 and 2) (US Government Printing Office, Washington D. C., December 1968).

James P. Palmer and Donald W. Spratt, "Pelvic Carcinoma Following Irradiation for Benign Gynecological Diseases," American Journal of Obstetrics and Gynecology 72: 497-505 (1956).

L. N. Parker, J. L. Belsky, T. Vamamoto, S. Kawamoto, and R. J. Keehn, "Thyroid Carcinoma After Exposure to Atomic Radiation. A Continuing Survey of a Fixed Population, Hiroshima and Nagasaki, 1958-1971," Annals of Internal Medicine 80: 600-604 (1974).

A. P. Polednak, A. F. Stehney, and R. E. Rowland, "Mortality Among Women First Employed Before 1930 in the US Radium Dial-Painting Industry," American Journal of Epidemiology 107: 179-195 (1978).

A. P. Polednak and E. L. Frome, "Mortality Among Men Employed Between 1943 and 1947 at a Uranium Processing Plant," Journal of Occupational Medicine 23: 169-178 (1981).

Dale L. Preston, Hiro Kato, Kenneth J. Kopecky, and Shoichiro Fujita, "Studies of the Mortality of A-Bomb Survivors. 8. Cancer Mortality 1950-1982," Radiation Research 111: 151-178 (1987).

Carol K. Redmond, Antonio Ciocco, J. William Lloyd, and Hugh W. Rush, "Long-Term Mortality Study of Steelworkers. VI. Mortality From Malignant Neoplasms Among Coke Oven Workers," Journal of Occupational Medicine 14: 621-629 (1972).

Michele Reyes, Gregg S. Wilkinson, Gary Tietjen, George L. Voelz, John F. Acquavella, and Robert Bistline, "Brain Tumors at a Nuclear Facility," Journal of Occupational Medicine 26: 721-724 (1984).

R. A. Rinsky, R. D. Zumwalde, R. J. Waxweiler, W. E. Murray, Jr., P. J. Bierbaum, P. J. Landrigan, M. Terpilak, C. Cox, "Cancer Mortality at a Naval Nuclear Shipyard," Lancet i: 231-235 (1981).

E. Ron and B. Modan, "Benign and Malignant Thyroid Neoplasms After Childhood Irradiation for Tinea Capitis," Journal of the National Cancer Institute 65: 7-11 (1980).

K. J. Rothman and J. D. Boice, Jr., Epidemiologic Analysis with a Programmable Calculator (U.S. Government Printing Office, Washington, D. C., 1979).

Kenneth J. Rothman, Modern Epidemiology (Little, Brown and Company, Boston, 1986).

G. Saccomanno, C. Yale, W. Dixon, O. Auerbach, and G. C. Huth, "An Epidemiological Analyses of the Relationship Between Exposure to Rn Progeny, Smoking, and Bronchogenic Carcinoma in the U-Mining Population of the Colorado Plateau-1960-1980," Health Physics 50: 605-618 (1986).

J. M. Samet, M. V. Morgan, R. W. Buechley, C. R. Key, and A. A. Valdivia, "Studies of Grants, New Mexico, Uranium Miners: Status as of December, 1982," in Epidemiology Applied to Health Physics, Proceedings of the Health Physics Society, January 9-13, 1983, CONF-830101 (National Technical Information Service, Springfield, Virginia, 1983), pp. 444-453.

J. M. Samet, D. M. Kutvirt, R. J. Waxweiler, and C. R. Key, "Uranium Mining and Lung Cancer in Navajo Men," New England Journal of Medicine 310: 1481-1484 (1984).

Irving J. Selikoff, E. Cuyler Hammond, and Herbert Seidman, "Mortality Experience of Insulation Workers in the United States and Canada, 1943-1976," Annals New York Academy of Sciences 330: 91-116 (1979).

R. Seltzer and P. E. Sartwell, "Ionizing Radiation and Longevity of Physicians," Journal of the American Medical Association 166: 585-587 (1958).

R. E. Shore, R. E. Albert, and B. S. Pasternack, "Follow-up Study of Patients Treated by X-Ray Epilation for Tinea Capitis, Resurvey of Post-Treatment Illness and Mortality Experience," Archives of Environmental Health 31: 17-24 (1976).

R. E. Shore, L. H. Hempelmann, E. Kowaluk, P. S. Mansur, B. S. Pasternack, R. E. Albert, and G. E. Haughie, "Breast Neoplasms in Women Treated with X-Rays for Acute Postpartum Mastitis," Journal of the National Cancer Institute 59: 813-822 (1977).

R. E. Shore, E. D. Woodward, B. S. Pasternack, and L. H. Hempelmann, "Radiation and Host Factors in Human Thyroid Tumors Following Thymus Irradiation," Health Physics 38: 451-465 (1980).

R. E. Shore, E. Woodward, N. Hildreth, P. Dvoretsky, L. Hempelmann, and B. Pasternack, "Thyroid Tumors Following Thymus Irradiation," Journal of the National Cancer Institute 74: 1177-1184 (1985).

R. E. Shore, N. Hildreth, E. Woodward, P. Dvoretsky, L. Hempelmann, and B. Pasternack, "Breast Cancer Among Women Given X-Ray Therapy for Acute Postpartum Mastitis," Journal of the National Cancer Institute 77: 689-696 (1986).

P. G. Smith and R. Doll, "Age- and Time- Dependent Changes in the Rates of Radiation-Induced Cancers in Patients with Ankylosing Spondylitis Following a Single Course of X-Ray Treatment," in Late Biological Effects of Ionizing Radiation (International Atomic Energy Agency, Vienna, 1978), Vol 1, pp. 205-218.

P. G. Smith and A. J. Douglas, "Mortality of Workers at the Sellafield Plant of British Nuclear Fuels," British Medical Journal 293: 845-854 (1986).

F. W. Spiers, H. F. Lucas, J. Rundo, and G. A. Anust, "Leukemia Incidence in the U. S. Dial Workers," Health Physics 44 (Suppl. No. 1): 65-72 (1983).

J. H. Stebbings, H. F. Lucas, and A. F. Stehney, "Mortality From Cancers of Major Sites in Female Radium Dial Workers," American Journal of Industrial Medicine 5: 435-459 (1984).

Robert C. Steppacher and Judith S. Mausner, "Suicide in Male and Female Physicians," Journal of the American Medical Association 228: 323-328 (1974).

George Talley, Los Alamos National Laboratory Industrial Hygiene Group, personal communication (August 20, 1987).

M. Tokunaga, J. E. Norman, M. Asano, S. Tokuoka, H. Ezaki, I. Nishimori, and Y. Tsuji, "Malignant Breast Tumors Among Atomic Bomb Survivors, Hiroshima and Nagasaki, 1950-74," Journal of the National Cancer Institute 62: 1347-1359 (1979).

Shoji Tokuoka, "Ovarian Neoplasms in Atomic Bomb Survivors," in Cancer in Atomic Bomb Survivors eds. Itsuzo Shigematsu and Abraham Kagan (Japan Scientific Societies Press, Tokyo, Plenum Press, New York, 1986), pp. 179-189.

H. Dennis Tolley, Sidney Marks, Jeff A. Buchanan, and Ethel S. Gilbert, "A Further Update of the Analysis of Mortality of Workers in a Nuclear Facility," Radiation Research 95: 211-213 (1983).

United Nations Scientific Committee on the Effects of Atomic Radiation, Sources and Effects of Ionizing Radiation. 1977 Report to the General Assembly (United Nations, New York, 1977) pp. 5.

G. van Kaick, D. Lorenz, H. Muth and A. Kaul, "Malignancies in German Thorotrast Patients and Estimated Tissue Dose," Health Physics 35: 127-136 (1978).

G. L. Voelz, H. Stebbings, L. H. Hempelmann, L. K. Haxton, and D. A. York, "Studies in Persons Exposed to Plutonium," in Late Biological Effects of Ionizing Radiation, Proceedings of a Symposium, Vienna, March 13-17, 1978, (IAEA, Vienna, 1978), pp. 353-367.

G. L. Voelz, G. S. Wilkinson, J. W. Healy, J. F. McInroy, and G. L. Tietjen, "Mortality Study of Los Alamos Workers with Higher Exposures to Plutonium," in Epidemiology Applied to Health Physics. Proceedings of the Health Physics Society, January 9-13, 1983, CONF-830101 (National Technical Information Service, Springfield, Virginia, 1983), pp. 318-327.

George L. Voelz, Robert S. Grier, and Louis H. Hempelmann, "A 37-Year Medical Follow-Up of Manhattan Project Pu Workers," Health Physics 48: 249-259 (1985).

J. K. Wagoner, V. E. Archer, B. E. Carroll, D. A. Holaday, and P. A. Lawrence, "Cancer Mortality Patterns Among U. S. Uranium Miners and Millers, 1950 Through 1962," Journal of the National Cancer Institute 32: 787-801 (1964).

J. K. Wagoner, V. E. Archer, F. E. Lundin, D. A. Holaday, and J. W. Lloyd, "Radiation as the Cause of Lung Cancer Among Uranium Miners," New England Journal of Medicine 273: 181-188 (1965).

J. K. Wagoner, "Leukemia and Other Malignancies Following Radiation Therapy for Gynecological Disorders," in Radiation Carcinogenesis: Epidemiology and Biological Significance, J. D. Boice and J. F. Fraumeni, Jr., Eds. (Raven Press, New York, 1984) pp. 153-159.

T. Wakabayashi, H. Kato, T. Ikeda, and W. J. Schull, "Studies of the Mortality of A-Bomb Survivors, Report 7. Part III. Incidence of Cancer of 1959-1978, Based on the Tumor Registry, Nagasaki," Radiation Research 93: 112-146 (1983).

H. E. Walburg, Jr., "Radiation-Induced Life Shortening and Premature Aging," in Advances in Radiation Biology, Vol. 5, eds. J. T. Lett and H. Adler (Academic Press, New York, 1975), pp. 145-179.

Noel S. Weiss, "Ovary," in Cancer Epidemiology and Prevention eds. David Schottenfeld and Joseph F. Fraumeni, Jr., (W. B. Saunders Co., Philadelphia, 1982) pp. 871-880.

Laurie Wiggs, "Conversation with J. N. P. Lawrence," Los Alamos National Laboratory memorandum HSE-14-87-33 to Los Alamos File (January 23, 1987a).

Laurie Wiggs, "Meeting with George Littlejohn (HSE-1)," Los Alamos National Laboratory memorandum HSE-14-87-56 to Los Alamos File (February 12, 1987b).

Laurie Wiggs, "Meeting with Louis Hempelmann Regarding Early Los Alamos Data," Los Alamos National Laboratory memorandum HSE-14-87-86 to Los Alamos File (March 9, 1987c).

Laurie D. Wiggs, Carol A. Weber, and Gregg S. Wilkinson, "Injury Mortality Among a Cohort of Nuclear Industry Workers," presented at the Society for Occupational and Environmental Health 1987 Annual Conference "Injury Control: Crossroads for the Health and Safety Professions," Bethesda, Maryland, April 6-8, 1987.

Gregg S. Wilkinson, George L. Voelz, John F. Acquavella, Gary L. Tietjen, Michele Reyes, Robert Brackbill, and Laurie Wiggs, "Mortality Among Plutonium and Other Workers at a Nuclear Facility," in Epidemiology Applied to Health Physics, Proceedings of the Health Physics Society, January 9-13, 1983, CONF-830101 (National Technical Information Service, Springfield, Virginia, 1983).

Gregg S. Wilkinson, Gary L. Tietjen, Laurie D. Wiggs, Warren A. Galke, John F. Acquavella, Michele Reyes, George L. Voelz, and Richard J. Waxweiler, "Mortality Among Plutonium and Other Radiation Workers at a Plutonium Weapons Facility," American Journal of Epidemiology 125: 231-250 (1987).

John L. Young, Jr. and Earl S. Pollack, "The Incidence of Cancer in the United States," in Cancer Epidemiology and Prevention, eds. David Schottenfeld and Joseph F. Fraumeni, Jr., (W. B. Saunders Company, Philadelphia, 1982), pp. 138-165.

APPENDICIES

APPENDIX A

LOS ALAMOS CODING INSTUCTIONS

Discussion in coding rooms must be kept to a minimum. Discussion of names or other personal information on these records is forbidden. Failure to comply with these rules may result in disciplinary action.

This information is strictly confidential. Discussion of this personal material among employees or with non-employees, inside or outside study headquarters, is prohibited. Violation of this rule comprises grounds for immediate dismissal.

Each analyst should take a drawer and place a card in the front with her name on it. Code the complete drawer before beginning another one.

Difficulties with the coding instructions or with individual records should be brought to the attention of the supervisor. Do not discuss this with other analysts.

Problems with records will be recorded on a comment sheet and turned into the supervisor on Friday of each week. Limit your comments to those that would aid an editor. Record discrepancies such as multiple SSNs or Z numbers. Note partial dates. Do not record missing information. This sheet replaces the remarks field.

Sign on to the computer according to the DATATRIEVE instructions. Each data analyst will sign on with their assigned password and three initials.

For the initial entry, the "enter editor" prompt will be passed by entering a blank and carriage return. The "Enter E" prompt will always be passed by entering a blank and carriage return.

A microfiche with an incorrect label across the top must have a paper clip attached to flag the record as having an error. Print the correct spelling (the name on the employee record) on the upper right hand corner of the outside fiche envelope. Identify the error as "ER Incorrect".

If duplicate microfiche are present for an individual, they should be placed together in one jacket. The record cards must clearly belong to the same individual to be considered duplicates. When doubt exists as to whether or not these record cards belong to the same individual, they should be brought to the supervisor's attention.

When an employee has duplicate employee records on one fiche, be sure to read all information available. When coding the date of hire and beginning job title, use the earliest information available. Use the latest information available to determine the date of termination, last job title, and education. See specific coding instructions for details. The job title fields must be recorded exactly as they appear in the records to avoid unnecessary errors. See specific instructions for these fields.

Personal knowledge of individuals is not to be used as a basis for coding decisions.

General Rules for Dates

These rules apply to birthdate, hiredate, termdate, and deathdate.

Record all dates as MM/DD/YYYY.

Missing dates - i.e. the information does not exist are recorded " " (blank).

Illegible dates are recorded "09-09-9999".

Partial dates:

A. If month (or month and day) is missing, enter "06/30/YYYY".

B. If day is missing and month and year are present, enter "MM/15/YYYY".

C. If year is missing, enter "09-09-9999".

"Blank" means information does not exist, for example, termination date for an active employee.

"09-09-9999" means information exists but is illegible or unknown, for example, an unrecorded birthdate.

STUDY NUMBER (SN)

Code: Blank, pass this field with a CR

LAST NAME (LN)

Code: Literal, alphabetic

INSTRUCTIONS:

Delete hyphens and embedded blanks, truncate if over 15 characters.

Where there are two distinct last names, usually Spanish or married females (i.e., Ortege Y Gasset, Moya Villareal, Smith-Jones), leave a blank between the two last names and drop hyphens or Y's.

Prepositions and/or articles preceding a last name (Von, Van Der, D', De) are closed up and apostrophes deleted.

Use the name currently used by the employee. When an employee changes his/her name, use the most recent version. Check the label on the microfiche, if it is not the most recent version of the name, attach a paper clip and print the correct name on the microfiche jacket.

FIRST NAME (FN)

Code: Literal and alphabetic

INSTRUCTIONS:

When only a first initial is given, enter only the initial. Use the most complete form of the first name.

Close up spaced first names and consider one name and code as such.

Examples include:

La Verne code "Laverne"

La Vonne code "Lavonne"

Le Roy code "Leroy"

MIDDLE INITIAL (MI-1, MI-2)

Code: Literal and alphabetic

INSTRUCTIONS:

Enter the middle initial literally. When no middle initial is given or when "NMN" exits, leave blank.

In the case where there is more than one middle initial, enter each in the proper field.

TITLE (TI)

Code: Literal, alphanumeric

INSTRUCTIONS:

Code title if the employee records give one.

SR = Senior

JR = Junior

2D = Second

3D = Third

4H = Fourth

If no title exists, enter a blank.

SOCIAL SECURITY NUMBER (SS)

Code: Numeric

INSTRUCTIONS:

Enter SSN as found in the employee records. When no complete (nine digits) social security number is present, or the number is illegible, enter nine 9's (999999999). Missing SSNs will be recorded as "blank". Use SSN on the employment application when multiple SSNs exist. If SSN is not on the application, use SSNs from other records. Refer to records in the following order:

1. Application
2. PSQ
3. Other records

BIRTHDATE (BD)

Code: Month (two digits), Day (two digits), Year (four digits).

09-09-9999 = Unknown

INSTRUCTIONS:

Birthdate will be recorded using two digits each for the month and day, and four digits for the year. The month and day, and the day and year, will each be separated by a dash. One digit months and days will be preceded by a zero (0).

Example: March will be recorded as 03

December will be recorded as 12

Days will be recorded:

June 5	05
June 15	15

In summary, a date like May 7, 1946 would be recorded as 05-07-1946. Incomplete dates: Missing month = "06-30-YYYY", Missing day (month present) = "MM/15/YYYY", Missing year = "09-09-9999".

STATE OF BIRTH (BP)

INSTRUCTIONS:

Code place of birth only when specifically designated as such. Do not assume birth place. Check employment application and PSQ.

City without designation of state is not sufficient for coding birthplace.

Code according to geographic code list that is attached.

Code U if unknown.

Alaska	AK
Alabama	AL
Arizona	AZ
Arkansas	AR
California	CA
Colorado	CO
Connecticut	CT
Delaware	DE
District of Columbia	DC
Florida	FL

Georgia	GA
Hawaii	HI
Idaho	ID
Illinois	IL
Indiana	IN
Iowa	IA
Kansas	KS
Kentucky	KY
Louisiana	LA
Maine	ME
Maryland	MD
Massachusetts	MA
Michigan	MI
Minnesota	MN
Mississippi	MS
Missouri	MO
Montana	MT
Nebraska	NB
Nevada	NV
New Hampshire	NH
New Jersey	NJ
New Mexico	NM
New York	NY
North Carolina	NC
North Dakota	ND
Ohio	OH
Oklahoma	OK
Oregon	OR
Pennsylvania	PA
Rhode Island	RI
South Carolina	SC
South Dakota	SD
Tennessee	TN
Texas	TX
Utah	UT
Vermont	VT
Virginia	VA
West Virginia	WV
Wisconsin	WI
Wyoming	WY
Foreign Born	FB

SEX (SEX)

Code: M Male

F Female

U Unknown, not able to determine

INSTRUCTIONS:

Use the sex on the employment application, PSQ, or other records. Names are not a basis for coding sex.

RACE (RACE)

Code: 0 Caucasian/White

1 Oriental/Asian

2 American Indian

3 Black

U Unknown/Unsure

INSTRUCTIONS:

Race can only be coded when positive designation is present. Do not code race on the basis of name. Search all available records, beginning with the PSQ, for a definite designation of race. If no positive designation of race is present, code a "U" (unknown). Caucasian/White (0) is only coded when "White", "Caucasian", "W", or "H" is present in the records. Oriental (1) can only be coded when records state "Chinese", "Korean", "Hawaiian", "Far Eastern", "Asian", "Philipino", "Japanese", "East Indian", or "Vietnamese." American Indian (2) can only be coded when records specifically designate "Indian", "I" or give the name of his or her tribe. Black can only be coded when "Black", "Negro", "B" or "Colored", is specifically designated. All individuals not coded as 0-3 are to be coded as "Unknown/Unsure". Ignore designations of race such as "Light" and "Dark", etc. "Red" may be coded as two (2); American Indian. "Yellow" may be coded as (1); Oriental. When race is identified as "A", code the individual "Oriental" = (1). "Spanish", "Mexican", or

"Hispanic" ("H") will be coded as zero (0), Caucasian/White, in this field. Spanish surname is not sufficient for the assignment of a race code, zero "0". In lieu of other designations of race, these individuals are coded as "Unknown/Unsure" = "U".

Place of birth or nationality is not sufficient to code race.

ETHNICITY (20 CHARACTERS)

Code: Literal

Enter literally any mention of ethnicity on the record. For example: "Spanish-American", "H", "Hispanic", "Italian", "SP. AM", etc. Individuals with no mention of ethnicity will be left blank. Surname is not a basis for coding this field.

EDUCATION (EC)

Code: U Unknown

1 Less than high school graduate

2 High school attendance - graduation not stated: Includes individuals with 4 years of high school (Example: 1950-1954); completion of the 12th grade: or some college attendance in a Jr. college, or university.

3 High school graduate. Includes only individuals with proof of graduation diploma or GED/HSE.

4 Associates degree (AA, AS) - AA/AS degree from Jr. college, college, or university.

5 College graduate (BS, BA, AB, BSE) (only when degree or graduation is specifically stated).

6 Graduate degree (Masters or Doctorate) (only when degree or graduation is specifically stated).

INSTRUCTIONS:

If education is listed as "None", code Unknown "U". Code highest level of academic educational attainment. Refer to the employment applications, transcripts and other educational records. "Some junior high" and "junior high school graduates" are coded as (1) less than high school graduate. Individuals who attended high school for 4 years (1950-1954), completed 12th grade, or attended college without proof of high school graduation or proof of higher level degree (AA, BA, MA, Ph.D.) will be coded as "2". Vocational training, beauty college, etc. will not be counted as college attendance.

High school graduate is coded (3) if any of the following are true:

A. The word diploma, grad or graduation appear

B. HSE - high school equivalency exam is recorded

C. GED - graduate equivalency diploma is noted

Individuals who hold an Associates degree (AA, AS) from a college, Jr. college or university will be coded as "4". Trade/Beauty/Business college certificates do not count.

Attainment of a college degree is not guaranteed by the appearance of the major field of study in the degree box. College graduate is coded (5) only if a degree is recorded or the word graduate appears. This must be a Bachelors level degree (BS, BA, BSE, etc.). Graduate degree (6) is only coded if the individual has completed a Masters or Doctoral degree. Graduate school attendance is coded a (5) when there is no proof of graduate degree attainment.

Anytime doubt exists about the correct code for education, enter "U".

Do not refer to degree lists or college books for the purpose of coding.

Z-NUMBER (ZN)

Code: Number

INSTRUCTIONS:

Delete the "Z" and enter the numerical portion of the Z-Number. Enter only those numbers preceded by a "Z" or denoted in the "Z-Number" field on the record. Handwritten "Z-Numbers" are acceptable. Missing or illegible Z-Numbers should be left blank.

Supply leading zeros for Z-Numbers with less than five digits. Example: Z = 123, enter "00123". Do not refer to the "Z-Number" books.

DATE OF HIRE (HD)

Code: Month, Day, Year

INSTRUCTIONS:

Use the standard coding rules for dates and code the earliest date of hire with the Los Alamos Scientific Laboratory of the University of California or "Project Y" or "Los Alamos" regardless of duty station. Assume hire date is with "Los Alamos" unless otherwise stated. Employment with the University of California at other facilities does not count and should not be coded. Employment with other contractors such as Zia, the Department of Energy (AEC, ERDA, DOE), etc. should not be coded. Hire dates before 1942 should be questioned. Do not use a hire date from a "letter of offer". Missing dates: "09-09-9999". Incomplete dates: missing month = "06-30-YYYY", missing day (month present) = "MM/15/YYYY", missing year = "09-09-9999".

FIRST JOB TITLE (FJT)

Enter exactly the first job title corresponding with the first date of hire for the employee. You may use a job title from the letter of offer. If a job title does not exist, enter a "U" for unknown. Take job titles from the records in the following order:

1. Change of status
2. Letter of offer
3. Other

Use "job title" including comments in parentheses. Example: "(trainee)". When job title is unavailable, use classification. Example: "Gen III".

DATE OF LAST TERMINATION (TD)

Code: Month, Day, Year

INSTRUCTIONS:

Use the standard coding rules for dates and code the date of the last official or effective termination. When that does not exist, use the last day worked. If that is not available, use "last day paid". (Do not code the "date submitted"). Transfer to other University of California facilities including Livermore is considered termination. If terminated employee returns to work and is an active employee, do not code the earlier termination date. A termination date is only recorded if it is designated as "terminated", "quit", "retired", "fired", or "severance", "rif" or "reduction in force".

Individuals on leave of absence or disability on the last date entered on their employment records will be considered "active" and recorded with a blank. Active employees will be coded with a "blank". If an individual died while employed and a date of death is noted, this date will be considered the termination date when no other term date exists.

If it is impossible to determine an individuals status at last entry on the employee records, or the last entry is dated earlier than 12-31-1972, enter "09-09-9999".

Former Laboratory employees who have become consultants are considered terminated when they leave regular Laboratory employment.

Illegible term dates are coded "09-09-9999".

Partial dates: Missing month 06-30-YYYY

Missing day MM/15/YYYY

Missing year 09-09-9999

LAST OR MOST RECENT JOB TITLE (LJT)

Enter exactly the last job title which corresponds to the last date of termination. When this is unavailable, use the last job title you can find. For active employees, code the most recent job title corresponding to the most recent date on the record. When job title is unavailable, code classification. Enter "U" for unknown or unsure.

APPENDIX B

Radiation Exposure Records and Acquisition of History

Almost from its inception in 1943, some operations at the Los Alamos Laboratory have included work with various types of radiation. The two major forms of radiation exposure include exposure to penetrating ionizing radiation primarily from x-rays and gamma rays and exposure to isotopes of plutonium. Collectively, the penetrating ionizing radiation has been called "external ionizing radiation" because it is capable of penetrating the skin into the body. The plutonium has been referred to as "internal radiation" because it gives off alpha rays that are only capable of traveling short distances and do not normally penetrate the skin. Therefore, plutonium is most hazardous when it is taken into the body via inhalation, ingestion, or a wound.

When the Laboratory opened in 1943, the techniques to measure radiation exposure were in an embryonic stage and many were not yet developed. Many of the techniques were subsequently developed at Los Alamos, such as the chemistry needed to detect small amounts of plutonium in urine, developed by Wright Langham (Hempelmann, 1987; Wiggs, 1987c; Langham, 1947).

In 1943 the only technology available for measuring external radiation exposures was the Victoreen pocket ionization chamber which was a personal monitoring device worn by persons working in areas thought to have the potential for exposure to radiation (Hemplemann, 1987; Wiggs, 1987c). These pocket ionization chambers consisted of a small air ionization chamber generally calibrated with x-rays. These meters had a bakelite wall that prevented the meters from reading low energy (less than 1 mev) beta radiations (Nickson, 1951). The limitations of these meters were that they were highly energy dependent and the information on the type of energy an individual was exposed to was not available (Littlejohn, 1987; Hempelmann, 1987; Wiggs, 1987a; Wiggs, 1987b; Wiggs, 1987c). Furthermore, these chambers were capable of giving false readings when dropped on the floor or otherwise treated roughly (Littlejohn, 1987; Hempelmann, 1987; Nickson, 1951; Lawrence, 1987; Wiggs, 1987a; Wiggs, 1987b; Wiggs, 1987c). Therefore, these readings could not be interpreted in a quantitative fashion, but could be interpreted as representing a potential for radiation exposure.

Early techniques for measuring exposure to plutonium and other internal emitters such as polonium (210) and uranium (235, 238, tuballoy) was to take nose swipes of the individual's nostrils and count the activity using a stationary alpha counter (Hempelmann et al., 1973; Hempelmann, 1987; Wiggs, 1987c). These measures indicated exposure, but because they were influenced by a number of unquantifiable parameters, such as whether an individual breathed through the nose or mouth, these were also unreliable for quantitative measures. They could, however, be used qualitatively as an indication that an individual worked in an area with potential exposure to plutonium or other alpha emitters (Hemplemann, 1987).

External Radiation

Pocket chambers were supplemented with and eventually replaced by film badges for the measurement of external ionizing radiation. When used as personnel monitoring devices, film badges were worn on the body and were used to estimate the radiation absorbed or passing into the body. The earliest film badges consisted of photographic film, which when developed became dark as a result of exposure to radiation. As the technology improved, shielding was placed over areas of the film to allow health physicists to separate and qualitatively differentiate energies of radiation. In the 1950's, film badge technology advanced to include an estimate of exposure to neutrons. These calculations were performed by technicians using microscopes to count neutron tracks in the film emulsion.

In January 1944, the medical director at Los Alamos, requested "strips of film to check exposure to radiation" from the Oak Ridge facility of the Manhattan Engineering District (Hempelmann, 1944a).

In May 1944, Los Alamos received a limited number of these badges which were distributed to personnel working in radiation areas (Hempelmann, 1944b).

In June 1944, the order of additional film from the Kodak Film Company was authorized (Warren, 1944); therefore, the use of film badges at Los Alamos began in 1944. A report (Dessauer, 1944) dated November of 1944 describes these earliest film badges.

> "In order to monitor gamma radiation on the human body, Mr. R. Wilsey and others developed and calibrated a standard film badge. It consists of a

type K Kodak x-ray dental film pack, surrounded by a 20 mil. lead foil in the form of a cross folded over the edges and placed into a badge. The badge walls are of 20 mil. brass, and slide apart. One is equipped with a safety pin and is marked by a letter and/or number for identification. To keep the film in position a piece of 40 mil. cardboard is inserted into the badge with the film. The proper order of the different layers in the badge is then as follows: front wall, lead cross, film pack, lead cross ears, cardboard, back wall (with safety pin).

For the calibration of these films Mr. Wilsey used a sample of 20 mg. of Ra mounted in a spherical aluminum container" (Dessauer, 1944).

In August 4, 1947, a letter described the film badges in use from 1944 to that time in this manner:

"In the past we have used three types of film in each badge. One is the Eastman Industrial Type K x-ray safety film (.01 - 6/0 r); the second is the Dupont D-2 special type x-ray film, which really consists of two films, one more sensitive than the other, together covering the range .13 to 30 r; and the third is the Adlux film made by Dupont also. The last is extremely insensitive and is used only in the region of large exposures (65 to 1500 r). Recently we have been using only the first mentioned Eastman film, since it does very well for the kind of exposures to which our personnel are subjected. In cases where an operation is considered at all hazardous, all the above films are used (Evans, 1947)."

As time passed, an increasing number of individuals wore film badges to monitor their exposure to external radiation, but it must be noted that during the earliest years the monitoring did not include everyone with the potential for exposure, a misclassification which would bias the results toward the null and reduce the ability to detect adverse health effects if they existed.

Records for pocket ionization chambers no longer exist in a centralized location. The only data for these pocket chamber measures are contained in the individual's personal medical record maintained orginally by the Laboratory's Health Group and currently stored with the complete medical records at the Laboratory's Occupational Medicine Group. Medical records for women employed at any time during the period April 1943 through February 1945 (a date originally thought to represent the beginning of film badge measurements) were reviewed and any mention of radiation exposure including pocket ionization chamber measurements was abstracted. These data have been used in conjunction with other data to designate radiation workers.

All of the film badge data beginning in 1944 through 1981 have been computerized by the Laboratory Dosimetry Group. The earliest data were "evaluated" to estimate the radiation dose in rems and make it more comparable to later dosimetry data (Littlejohn, 1987). The external radiation data are in units known as rem, roentgen equivalent man, which is a "unit of dose equivalent" (Casarett, 1968). This unit is used to convert absorbed dose, measured in rads, into a unit that takes into account the fact that different types of radiation produce different degrees of biological response at the same level of energy deposition in living tissue. Quality factors are used to standardize the dose against the equivalent dose from gamma rays produced by cobalt-60. The rem is a measure used widely for radiation protection activities (Casarett, 1968).

In 1980, the Los Alamos Laboratory switched to the thermoluminescent dosimeter (TLD) to measure external radiation data. These TLDs contain lithium flouride crystals which store energy when exposed to radiation. When heated, these crystals give off light, a measure of which is used to quantify radiation exposure (Casarett, 1968). Like film badges, TLDs are shielded to allow different types of radiations to be measured. These monitors are especially good for measuring exposures to neutrons.

In addition to exposures received at Los Alamos, the computerized dosimetry data included information on previous exposures and exposures received at other facilities and test sites visited by Laboratory employees. These values were included in the lifetime exposures of persons employed by the Laboratory. As with many things, this procedure was not always followed in the earliest days of monitoring, but has been strictly and consistently followed since the 1950's. Also included in the computerized radiation records were the film badge measurements for personnel monitored at the Trinity Test, when the first atomic bomb was detonated (Littlejohn, 1987).

The computerized external radiation data were obtained from the Laboratory's Dosimetry Group and a large effort was undertaken to match these data against the cohort of women employed by the Laboratory. Many problems, related to the limited identifying data on the radiation record, were encountered. Computerized matches on z-number were made first followed by name and date matches. All discrepancies or questionable matches were resolved by hand, through review of the personnel records to determine if the individual in the radiation record was the same as in the cohort.

Because the computerized radiation records contained annual exposure summaries, important dates, such as the first sample date, had to be estimated. For example, if an individual was first monitored in the same year she was hired, the first sample date was established as the midpoint between the hire date and the end of the hire year. If an individual was first monitored in her termination year, the first sample date was established as the midpoint between the first day of the termination year and the actual termination date. If the first sample date occurred during a nonhire/nontermination year of the individual's employment, the first sample date was established as the midpoint of the year. Persons with radiation exposures from previous employments were assigned a first sample date equivalent to their hire date. Dates on which an individual attained her first positive sample and cumulative radiation doses of 1, 5, and 10 rem were also calculated. These dates were estimated from the annual exposure records in the same fashion as the first sample date. Persons with previous positive radiation exposures or exposures of at least 1 rem, 5 rems or 10 rems were assigned their hire date for the corresponding dose category. Cumulative radiation dose for an individual from hire date through termination or the EOS, December 31, 1981, was also calculated for monitored study subjects.

Plutonium

Plutonium was first discovered in late 1940 by Glenn T. Seaborg and his colleagues at Berkeley (Seaborg, 1963). In 1944, Dr. Seaborg, recognizing the potential health risks from plutonium, provided 10 milligrams of the first half gram of plutonium in the world to the Crocker Radiation Laboratory for biological and metabolic experiments. Dr. Seaborg recognized that plutonium and radium possessed similar radioactive properties (Hempelmann et al., 1973).

Radium was already known to cause bone cancer from the 1920's experience of the radium dial painters (Martland et al., 1925; Martland et al., 1929).

In the spring of 1944, the first milligram quantities of plutonium arrived at Los Alamos. Because plutonium was considered to be potentially hazardous, safety regulations were instituted when plutonium chemistry work began at Los Alamos. For example, workers wore coveralls, "booties" (shoe covers), and surgical caps while in the work place. Workers were required to shower and turn in their work coveralls when leaving "D Building", the wooden building in which all plutonium work was originally conducted. Nevertheless, work place exposures to plutonium were inevitable (Hempelmann et al., 1973).

Early surveillance procedures consisted of daily monitoring of each laboratory with additional monitoring in the event of an accident. Routine monitoring consisted of wiping Laboratory work surfaces with "lightly oiled filter paper". The radioactivity of the filter papers was then counted in a stationary proportional alpha counter. Decontamination procedures were used in areas considered to be highly contaminated based on the results of this monitoring (Hempelmann et al., 1973).

Personal monitoring (in contrast to work area monitoring) initially consisted of the nose swipes already mentioned. In 1944, monitoring was expanded to include a program to collect urine samples after the worker had his/her decontamination shower. The initial purpose of these early urine samples was for Wright Langham's use in developing a chemical method for the separation of plutonium from urine (Campbell et al., 1972).

By March of 1945, Langham had developed a urine bioassay technique that allowed crude estimates of plutonium body burden (Hempelmann et al., 1973). March of 1945 represented the initiation of the formal urine bioassay program at Los Alamos. Because contamination of the urine samples was a major concern, an elaborate monitoring procedure, the "Health-Pass Ward", was established. Employees were given a pass and sent out of Los Alamos for two days. When the employee returned to Los Alamos, they reported to the hospital where they showered and entered a hospital ward. Urine output was collected for the next 24 hours after the first urine had been discarded (Hempelmann, 1987; Campbell et al., 1972). Eventually, the monitoring procedure was changed and the health pass program was eliminated due to the great cost in time and money required to give employees three days off each time a urine bioassay was required (Hempelmann, 1987; Campbell et al., 1972). Today, employees take home four disposable glass bottles and collect four urine outputs. These "kits" are then returned to the Laboratory for analyses (Campbell et al., 1972).

As mentioned above, a technique to separate plutonium from the urine and estimate body burden came into use in 1945. Extensive experimentation continued to revise and improve the estimation of body burden from urine bioassay. Human experimentation included injecting known quantities of plutonium citrate into terminally ill individuals and measuring the plutonium recovered from the urine (Langham, 1951).

Based on this human experimentation, Langham developed an equation to describe the relationship of plutonium in the urine and plutonium in the body. Many models have been based on the Langham equation. A computer code, PUQFUA, was developed at Los Alamos in 1959. This code uses the Langham equation plus detailed information on the Laboratory techniques and error rates during the history of plutonium bioassay operations at Los Alamos. Elaborate correction factors and validation procedures are incorporated in this code (Lawrence, 1978). The version of the code (PUQFUA III) in use today also incorporates results of an autopsy study under way at Los Alamos. The autopsy study, under the direction of Dr. James McInroy, is analyzing human tissues to estimate the amount and patterns of deposition of plutoniun in human tissues (McInroy, 1976; McInroy et al., 1979). Some of the individuals autopsied were bioassayed during their lifetime and the results of the tissue analyses have been compared with the urine estimates. The PUQFUA III code has been adjusted to increase the agreement between urine and autopsy results (Lawrence, 1987).

Plutonium body burdens, a measure of plutonium deposited in the body, are calculated at Los Alamos annually using the current PUQFUA III code. Data for each urine bioassay for every individual (n >9500) monitored at Los Alamos since 1945 are entered into the PUQFUA III program which calculates a current estimate of plutonium body burden based on the latest excretion model.

The 1986 plutonium body burden data were obtained and matched to the cohort. For each individual bioassayed, the following variables were abstracted: first bioassay date, the isotope of plutonium, the number of valid bioassay samples (samples that do not meet the stringent validity checks in the model are considered not valid), last bioassay date for plutonium, the current estimate of nanocurie-years, the nanocurie-years at the last sample, the previous body burden estimate, and the current body burden estimate. Plutonium body burden estimates are measured in nanocuries (nCi). The current maximum permissable body burden (MPBB) is set at 40 nCi (International Committee on Radiation Protection, 1959). Nanocurie-years is a time related measure of body burden. This concept is important because due to the very long biological half life of plutonium, a person is continually exposed to plutonium once it has been taken into the body. The nanocurie-year measure is an attempt to consider this biologically important characteristic of plutonium. The total nanocurie-years for an individual are the product of the incremental body burden times the number of years since the uptake, summed across all incremental measurements (Lawrence, 1978).

A first positive sample date was hand calculated for each bioassayed study subject. Detailed records containing each bioassay for an individual were reviewed. These detailed records contain a urine activity value in counts or disintegrations per minute (depending on the historical time period). Correction factors for background activity were applied to each measurement for the individual. The correction factors differed across three time periods. Each sample was reviewed and the appropriate correction factor for the date of the sample was subtracted. If the value was still a positive number, this was determined to be a positive uptake. The date of the first positive uptake was recorded for the individual.

REFERENCES

Alison P. Casarett, Radiation Biology (Prentice-Hall, Inc., Englewood Cliffs, New Jersey, 1968) pp. 32-41, 268-273.

Evan E. Campbell, Morris F. Milligan, William D. Moss, and Harry F. Schulte, "History of the Plutonium Bioassay Program at the Los Alamos Scientific Laboratory, 1944-1972," Los Alamos Scientific Laboratory report LA-5008 (October 1972).

Gerhard Dessauer, "Film Monitoring of Gamma Rays on the Human Body," unpublished (November 2, 1944).

Cerda D. Evans, Los Alamos Scientific Laboratory, letter to Dr. Joe W. Howland, University of Rochester, August 4, 1974.

L. H. Hempelmann, M.D., P.O. Box 1663, Santa Fe, letter to Col. Stafford L. Warren, Army Service Forces, United States Engineer District, Oak Ridge, Tennessee, January 19, 1944.

L. H. Hempelmann, M.D., P.O. Box 1663, Santa Fe, letter to Col. Stafford L. Warren, Army Service Forces, United States Engineer District, Oak Ridge, Tennessee, May 18, 1944.

L. H. Hempelmann, W. H. Langham, C. R. Richmond, and G. L. Voelz, "Manhattan Project Plutonium Workers: A Twenty-Seven Year Follow-Up Study of Selected Cases," Health Physics 25: 461-479 (1973).

L. H. Hempelmann, University of Rochester School of Medicine (retired), personal communication (February 11, 1987).

International Commission on Radiation Protection, "Report of Committee II on Permissible Dose for Internal Radiation (1959)," Health Physics 3: 1-40, 1959.

Wright H. Langham, "Determination of Plutonium in Human Urine," Los Alamos Scientific Laboratory report LAMS-603 (August 14, 1947).

Wright H. Langham, "The Application of Excretion Analyses to the Determination of Body Burden of Radioactive Isotopes," British Journal of Radiology, Supplement 7, Part V: 95-113 (1951).

James N. P. Lawrence, "A History of PUQFUA: Plutonium Body Burden (Q) from Urine Assays," Los Alamos Scientific Laboratory report LA-7403-H (October 1978).

J. N. P. Lawrence, "Some Further PUQFUA Studies," in Proceedings of the Department of Energy Workshop on Radiobioassay and Internal Dosimetry, Albuquerque, New Mexico, January 20-22, 1986, PNL-SA-14043, CONF-860146, UC-41 (Pacific Northwest Laboratory, Richland, Washington, 1987).

George Littlejohn, Los Alamos National Laboratory (retired), personal communication (February 2, 1987).

H. S. Martland, P. Conlon, and J. P. Knef, "Some Unrecognized Dangers in the Use and Handling of Radioactive Substance, "Journal of the American Medical Association 85: 1769-1776 (1925).

H. S. Martland, "Occupational Poisoning in Manufacture of Luminous Watch Dials," Journal of the American Medical Association 92: 466-473 (1929).

J. F. McInroy, "The Los Alamos Scientific Laboratory's Human Autopsy Tissue Analysis Study," in The Health Effects of Plutonium and Radium ed. Webster S. S. Jee (J. W. Press, Salt Lake City, Utah, 1976).

J. F. McInroy, E. E. Campbell, W. D. Moss, G. L. Tietjen, B. C. Eutsler, and H. A. Boyd, "Plutonium in Autopsy Tissue: A Revision and Updating of Data Reported in LA-4875," Health Physics 37: 1-136 (1979).

J. J. Nickson, "Protective Measures for Personnel" in Industrial Medicine on the Plutonium Project, Survey and Collected Papers ed. Robert S. Stone (McGraw-Hill Book Company, Inc., New York, New York, 1951) p. 110.

Glenn T. Seaborg, Man-Made Transuranium Elements (Prentice-Hall, Inc., Englewood Cliffs, New Jersey, 1963), p. 9.

Stafford L. Warren, Army Service Forces, United States Engineer District, Oak Ridge, Tennessee, letter to Louis H. Hempelmann, P. O. Box 1663, Santa Fe, New Mexico, June 14, 1944 (unclassified 7/3/79).

Laurie Wiggs, "Conversation with J. N. P. Lawrence," Los Alamos National Laboratory memorandum HSE-14-87-33 to Los Alamos File (January 23, 1987a).

Laurie Wiggs, "Meeting with George Littlejohn (HSE-1)," Los Alamos National Laboratory memorandum HSE-14-87-56 to Los Alamos File (February 12, 1987b).

Laurie Wiggs, "Meeting with Louis Hempelmann Regarding Early Los Alamos Data," Los Alamos National Laboratory memorandum HSE-14-87-86 To Los Alamos File (March 9, 1987c).