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Morbidity and Mortality in Los Alamos County, New Mexico

I. Methodological Issues and Preliminary Results[1]

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Cancer among Los Alamos County, New Mexico, male residents, all of whom have worked in or have lived within a few kilometers of a major plutonium plant and other nuclear facilities, has been reviewed with respect to mortality between 1950 and 1969 and incidence between 1969 and 1974. A possible excess of neoplasms of the reticuloendothelial system was detected, but the incidence data suggest that this excess, if real, is no longer occurring. Several potentially causal occupational exposures have existed. Higher than expected incidence, currently, of cancers of the colon and rectum appears to be explained better by socioeconomic than occupational factors. Neither mortality nor incidence data suggest an excess of lung cancer in Los Alamos males. Healthy worker and healthy military effects, white ethnicity, and migration are discussed as intervening variables relevant to interpreting mortality data in counties dominated by a single major facility. The utility of county data bases in the study of single local area mortality rates is reviewed.

INTRODUCTION

The health of residents of communities which have developed with the nuclear industry is of current interest as society considers the role of nuclear power in the world's energy future. Los Alamos County, New Mexico, is such a community, and one in which exposures to plutonium, as well as to external ionizing radiation, have occurred.

Los Alamos was selected during World War II as the site for the laboratory to develop the first atomic bomb. The population has since grown continuously, to over 15,000 persons in the 1970s. The principal employer remains the Los Alamos Scientific Laboratory, and the great majority of the employed population work in the nuclear industry. Some residential areas of the town are located within a few hundred meters of chemical laboratories and radiation areas, including major plutonium facilities. Residential development began very near the original technical area and has since spiraled outward.

The Health Division of the Los Alamos Scientific Laboratory initiated these studies of cancer incidence and mortality in Los Alamos County in the hope of gaining leads to any health effects associated with radiation or chemicals. As one of the first tasks for the scientists, technicians, and craftsmen at Los Alamos was to develop methods to process and fabricate the newly discovered element, plutonium, and since hundreds of persons have continued to work with plutonium

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through the years, a major emphasis in these studies is on plutonium. Voelz *et al.* have published clinical (1979) and preliminary epidemiologic (1978) results on subjects occupationally exposed to plutonium.

This paper presents some preliminary results on the mortality experience of the Los Alamos County male population, and presents in detail the methodological aspects of the county mortality study both to prepare the groundwork for future substantive contributions concerning the Los Alamos County population and because methodology is central to the concern of this "Workshop on Health Surveillance around Point Sources of Pollution."

Los Alamos County is at one extreme of communities affected by a "point source." It has no past, no comparable neighboring populations, and nearly the entire male population (and a large fraction of the females) has been employed at the "point source."

The ideal situation for monitoring health effects in residents around a point source is where the employees of the source are a very small fraction of the resident population, where prior health data for the area can be developed, and where the polluting facility is introduced into a physically large, homogeneous region (a Midwestern agricultural county, or a residential neighborhood in a large urban area, as examples). In this latter situation the study area can be compared with a large, comparable, contiguous region both before and after the pollutant source becomes operational.

Los Alamos, however, arose *de novo*, the residentially exposed are mostly the occupationally exposed, and the neighboring Indian and Spanish populations are in no way comparable to the highly educated Anglo newcomers of Los Alamos County. This paper is an investigation of what can be done under such circumstances.

METHODS

In this paper we report cancer mortality and preliminary cancer incidence data for males, and include limited results for females only for methodologic purposes.

Cancer mortality rates are from Mason and McKay's (1974) "U.S. Cancer Mortality by County: 1950–1969" and some data on corresponding statistical significance levels are taken from Mason *et al.*'s (1975) "Atlas of Cancer Mortality for U.S. Counties: 1950–1969."

These cancer rates for white males in Los Alamos County are compared with rates from both the state of New Mexico and from the United States as a whole. In addition, white male cancer rates in five socioeconomic and occupational control counties and in five high education Western counties are compared with the rates in Los Alamos County.

The two counties most closely bracketing Los Alamos County with respect to four criteria, median education, median family income, percent professional and managerial, and percent government employees, were selected from among all counties meeting the preliminary eligibility criteria of a population above 5000 and a median income rank less than 1000. Because of correlation among attributes, this process yielded five rather than eight counties: Pitkin, Colorado; Montgomery, Maryland, Mineral, Nevada; Tooele, Utah, and Fairfax, Virginia.

From the remaining eligible counties all Western counties with a median education greater than or equal to 12.8 years for persons aged 25 and above were selected. These were: Marin, California; Boulder, Colorado; Benton, Oregon; Whitman, Washington; and Albany, Wyoming.

Demographic and socioeconomic characteristics of counties were from the 1970 United States census, published in the Bureau of the Census's (1973) "City and County Data Book, 1972." Altitudes of the county seats (of the largest city for Fairfax) were from the "Commercial Atlas and Marketing Guide" (1977).

Data on cancer incidence in Los Alamos County were obtained from the New Mexico Tumor Registry of the Cancer Research and Treatment Center at the University of New Mexico. Rates for Los Alamos County are compared to rates from Bernalillo County (Albuquerque) and for the entire state of New Mexico, data for Anglo-white males only being utilized for all areas.

Tests of significance for cancer mortality are either from Mason *et al.* (1975) based on a method of Chiang (1961) for age-adjusted rates, or, since observed numbers for Los Alamos County are invariably small, on a method given by Haenszel *et al.* (1962) based on the Poisson distribution.

In this series of papers describing county-level statistics, we have not attempted to quantify either the occupational or the residential exposures to which the county residents have been exposed. In principle, samples from residential lists could be matched with health physics records, or ambient population exposures estimated for past years. However, we have ongoing a series of case-control studies of cancer in Los Alamos County residents in which individual occupational exposures and neighborhood of residence are investigated for both cancer cases and individually matched controls. These are in addition to our major study, an occupational cohort study of plutonium workers at Los Alamos and other sites. The formidable task of generating county-level estimates for a 30-year period would defeat the purpose of county-level studies, which is to serve as simple screens for worthwhile hypotheses for more intensive investigations.

Reports are available concerning radioactive air pollution (Jordan and Black, 1958) and soil contamination by plutonium (Kennedy and Purtymun, 1971a, b; Johnson, 1972). A recent radiological survey of the former main technical area, near which residential development began has also been published (Ahlquist *et al.*, 1977).

RESULTS

The characteristics of Los Alamos County and control counties are shown in Table 1. Los Alamos County, on the 1970 census, had the second highest average levels of education and income in the United States and was top in percent professional and managerial and percent government employees. The latter two variables are not well matched by the control counties. The high-education control counties do not closely approach Los Alamos in income or characteristics of employment.

It should also be observed that each set of control counties is made up of a minority of very large counties themselves part of much larger Standard Metropolitan Statistical Areas, and a majority of small to very small counties.

TABLE I

CHARACTERISTICS OF LOS ALAMOS COUNTY, NEW MEXICO, AND CONTROL COUNTIES[a]

County	Altitude[b] (meters)	Population 1970 (10^3)	Median education (years)	Median family income ($)	Professional & managerial (%)	Government employees (%)
Los Alamos, N.M.	2225	15	14.2	15,153	60.0	70.5
Socioeconomic and occupational control counties[c]						
Pitkin, Colo.	2418	6	14.4[d]	11,763	31.4	9.2
Montgomery, Md.	137	523	13.0[d]	16,708[d]	47.0[d]	33.7
Mineral, Nev.	1317	7	12.2	10,172	19.3	60.5[d]
Tooele, Utah	1530	22	12.3	9,723	24.8	61.4[d]
Fairfax, Va.[e]	107	599	~12.85	~14,821[d]	~41.6[d]	~38.9
High-education Western control counties[f]						
Marin, Calif.	10	206	12.9	13,931	39.2	18.2
Boulder, Colo.	1634	132	12.8	11,196	37.0	25.3
Benton, Oreg.	68	54	12.9	9,642	35.2	38.7
Whitman, Wash.	998	38	12.8	9,099	33.1	42.8
Albany, Wyo.	2183	26	12.9	8,535	34.8	42.0

[a] Demographic data from "City and County Data Book" (Bureau of the Census, 1973) for 1970. All control counties, chosen from 3141 U.S. counties, have a population ≥5000 and a median income rank ≤1000.

[b] Altitude of county seat (for Fairfax, of largest city), from "Commercial Atlas and Marketing Guide" (1977).

[c] Next higher and next lower (or two next lower where necessary) counties with respect to: median education of persons aged 25 and above ("City and County Data Book" (CCDB), Table 2, col. 24); median family income (CCDB, Table 2, cols. 58, 59); professional and managerial white collar workers as a percentage of civilian employed (CCDB, Table 2, col. 44); and government workers as a percentage of civilian employed (CCDB, Table 2, col. 45).

[d] Criteria by which these socioeconomic and occupational control counties were selected.

[e] Averages of characteristics weighted by persons aged 25 and above, families, or civilian employed, as applicable, for Fairfax County and for the independent cities of Alexandria, Fairfax, and Falls Church, the grouping corresponding with "Fairfax" in Mason and McKay (1974).

[f] Western counties with median education ≥12.8 years for persons aged 25 and above, and not included among the socioeconomic and occupational control counties.

White male mortality rates for major cancer sites for Los Alamos County and the two groups of control counties are given in Tables 2 and 3. A high degree of variability in rates, due in part to small population sizes, is evident in these presumably well-matched sets of counties.

It is difficult to draw inferences from such large tabulations and these data are summarized in Table 4, which gives magnitude, and Table 5, which gives statistical significance. Rates for New Mexico in Table 4 have a large Hispanic component and are consequently not used for significance testing in Table 5. Although some probability levels are given for the control county comparisons, these comparisons essentially contribute consistency to the statistical tests against national rates. The problems in utilizing control counties for significance testing will be discussed below.

Table 5 most clearly summarizes the findings concerning cancer in Los Alamos males. Los Alamos clearly is a county of extremes, being the extreme or next to extreme case in all comparisons except with respect to brain and total neoplasms. It is also clear that Los Alamos is low as often as high, and that a higher level of statistical significance attaches to the low values than to the high.

Cancers of the digestive system, except liver, are consistently low: expected values for stomach and for large intestine/rectum are sufficiently large that these results are statistically significant.

Lung cancer has been notably and statistically significantly low during this period, despite the fact that the highest index of suspicion would attach to this site in plutonium-exposed workers or populations.

Prostatic and bladder cancer were high, but not statistically significantly high, due, in part, to the small numbers of deaths.

Lymphosarcoma and leukemia looked at separately were high, but not statistically significantly high. Because the total number of deaths involved, 10, was sizable, we decided to consider all cancers of lymphatic and hematopoietic tissue. We observed 15: 2 Hodgkin's, 4 lymphosarcoma, 3 multiple myeloma, and 6 leukemia. A total expected was computed from available published data, summing: (the observed cause-specific deaths) × ((The U.S. age-adjusted rate) / (the Los Alamos County age-adjusted rate)). This yielded 9.2 expected cases and a standard mortality ratio of 163. By the method of Haenszel *et al.* (1962) the lower limit of the 95% confidence interval is 0.913. Although not statistically significant, this excess of cancers of the lymphatic and hematopoietic system must be considered a suspect, borderline finding.

Although significance levels for "all malignant neoplasms" are presented in Table 5, it is clear that extreme heterogeneity among cancers exists and that significance testing or discussions of rates of all cancers combined have no substantive scientific meaning.

Table 6 presents recent cancer morbidity data for Los Alamos County Anglo males, obtained from the New Mexico Tumor Registry.

Cancers of the digestive tract are high compared to rates in either Albuquerque or the entire state, contrary to the mortality findings presented above. The standardized morbidity ratios for cancer of the large intestine are 2.35 relative to New Mexico, 2.02 relative to Albuquerque. Statistically significant elevation is

TABLE 2

WHITE MALE MORTALITY RATES FOR MAJOR CANCER SITES, LOS ALAMOS COUNTY AND SOCIOECONOMIC AND OCCUPATIONAL CONTROL COUNTIES, 1950 – 1969[a]

	Los Alamos, N.M.[b]	Pitkin, Colo.	Montgomery, Md.	Mineral, Nev.	Tooele, Utah	Fairfax, Va.
Stomach	3.5 (3)	11.7	9.7	7.0	12.7	11.3
Large intestine	8.8 (4)	25.5	19.1	6.4	11.3	15.3
Rectum	2.8 (2)	0.0	6.5	5.2	4.7	5.2
Biliary passages and liver	6.3 (2)	0.0	4.2	3.9	1.0	4.2
Pancreas	1.0 (1)	10.5	9.8	10.3	9.4	8.9
Trachea, bronchus, and lung	12.0 (8)	36.8	38.9	45.0	39.0	44.6
Prostate	30.3 (3)	19.1	19.4	17.2	25.8	17.9
Bladder	15.7 (3)	0.0	7.8	12.7	4.8	7.1
Brain and other parts of nervous system	4.9 (5)	3.4	5.8	0.0	2.0	4.3
Lymphosarcoma and reticulosarcoma, etc.	7.1 (4)	2.7	6.0	1.6	4.4	4.3
Leukemia	16.3 (6)	3.8	9.2	9.1	8.8	8.2
All malignant neoplasms						
Rate	142.6	165.0	175.0	168.1	159.4	173.1
Number	54	32	3485	85	180	2794

[a] Direct age-adjusted average annual rates per 100,000 population, 1950 – 1969 from Mason and McKay (1974).

[b] Number of cases, 1950 – 1969, in parentheses.

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TABLE 3

WHITE MALE MORTALITY RATES FOR MAJOR CANCER SITES, LOS ALAMOS COUNTY AND HIGH-EDUCATION WESTERN CONTROL COUNTIES, 1950–1969[a]

	Los Alamos, N.M.	Marin, Calif.	Boulder, Colo.	Benton, Oreg.	Whitman, Wash.	Albany, Wyo.
Stomach	3.5	13.2	10.9	10.9	13.8	12.4
Large intestine	8.8	15.2	10.2	11.5	16.4	16.0
Rectum	2.8	8.4	4.7	5.1	5.1	8.1
Biliary passages and liver	6.3	3.7	4.0	4.3	4.2	4.3
Pancreas	1.0	10.6	8.8	7.0	12.0	8.1
Trachea, bronchus, and lung	12.0	37.5	26.2	27.3	22.4	18.6
Prostate	30.3	18.9	16.8	20.6	17.6	22.8
Bladder	15.7	8.0	5.5	5.7	6.4	7.5
Brain and other parts of nervous system	4.9	4.3	2.5	7.9	4.0	2.3
Lymphosarcoma and reticulosarcoma, etc.	7.1	5.8	6.2	4.5	4.2	1.3
Leukemia	16.3	9.0	9.0	9.6	11.4	10.4
All malignant neoplasms						
Rate	142.6	173.9	134.7	141.2	142.3	148.1
Number	54	1880	855	405	411	227

[a] Direct age adjusted average annual rates per 100,000 population, 1950–1969 from Mason and McKay (1974).

TABLE 4
MORTALITY RATES FOR MAJOR CANCER SITES IN LOS ALAMOS WHITE MALES COMPARED TO RATES IN CONTROL AREAS, 1950–1969*

	Socioeconomic and occupational controls (range)	High-education, Western controls (range)	*Los Alamos County*	New Mexico	United States
Stomach	7.0–13.7	10.9–13.8	*3.5*	17.96	15.22
Large intestine	6.4–25.5	10.2–16.4	*8.8*	9.15	16.54
Rectum	0.0–6.5	4.7–8.4	*2.8*	3.39	7.65
Biliary passages and liver	0.0–4.2	3.7–4.3	*6.3*	5.33	5.16
Pancreas	8.9–10.5	7.0–12.0	*1.0*	8.79	9.63
Trachea, bronchus, and lung	36.8–45.0	18.6–37.5	*12.0*	24.71	37.98
Prostate	17.2–25.8	16.8–22.8	*30.3*	15.87	17.84
Bladder	0.0–12.7	5.5–8.0	*15.7*	3.97	6.78
Brain and other parts of nervous system	0.0–5.8	2.3–7.9	*4.9*	3.30	4.42
Lymphosarcoma and reticulosarcoma, etc.	1.6–6.0	1.3–6.2	*7.1*	3.64	4.89
Leukemia	3.8–9.2	9.0–11.4	*16.3*	7.71	8.81
All malignant neoplasms	159.4–175.0	134.7–173.9	*142.6*	136.30	174.04

* Direct age-adjusted average annual rates per 100,000 population, 1950–1969 from Mason and McKay (1974).

suggested by the corresponding lower 95% confidence limits, 1.17 and 1.01 (based on the method of Haenszel *et al.*, 1962). The corresponding standardized morbidity ratios for all cancer of the digestive tract are 2.33 and 2.02 (lower 95% confidence limits 1.48 and 1.28).

Incidence rates for lung cancer during this 1969–1974 period were not low, as mortality rates had been through 1969, but there is no suggestion that they are elevated during this period.

Leukemia and lymphoma incidence rates were clearly not above expected during this period, even though mortality results had suggested excesses in the 1950–1969 period.

Rates of cancer in Los Alamos females, who are occupationally exposed to a much lesser degree than males, assist in interpreting the preceding findings. Table 7 presents cancer morbidity and mortality data for females for sites of particular interest in the male analyses.

It can be seen that cancers of the digestive system have been occurring in Los Alamos County females from the beginning at the expected rates, although the males were significantly low during this 1950–1969 period. Both sexes currently show an excess incidence of cancer of the large intestine.

Females showed a slight excess of lung cancer during the 1950–1969 period, but incidence rates are currently low. Males had been low during the 1950–1969 period, but current lung cancer rates are average.

Leukemias and lymphosarcomas were low in females in the 1950–1969 period.

TABLE 5
RANK AND STATISTICAL SIGNIFICANCE OF WHITE MALE MORTALITY RATES IN LOS ALAMOS COUNTY, 1950–1969

	Rank[a] of rates in Los Alamos Co. relative to				
	Socioeconomic and occupational controls ($n = 6$)	High-education Western controls ($n = 6$)	Combined controls ($n = 11$)	Probability of rank ($n = 11$) High	Probability of rank ($n = 11$) Low
Stomach	6	6	11		0.091
Large intestine	5	6	10		0.182
Rectum	5	6	10		0.182
Biliary passages and liver	1	1	1	0.091	
Pancreas	6	6	11		0.091
Trachea, bronchus, and lung	6	6	11		0.091
Prostate	1	1	1	0.091	
Bladder	1	1	1	0.091	
Brain and other parts of nervous system	2	2	3	0.273	
Lymphosarcoma and reticulosarcoma, etc.	1	1	1	0.091	
Leukemia	1	1	1	0.091	
All malignant neoplasms	6	4	7		0.455

	Significance[b] of difference between Los Alamos County and U.S. white cancer rates		
	Direction	Mason and McKay[c]	Poisson[d]
Stomach	Low	$P < 0.05$	$P < 0.05$
Large intestine	Low	$P < 0.05$	NS
Rectum	Low	$P < 0.05$	NS
Biliary passages and liver	High	NS	NS
Pancreas	Low	$P < 0.05$	$P < 0.05$
Trachea, bronchus, and lung	Low	$P < 0.05$	$P < 0.05$
Prostate	High	—[e]	NS
Bladder	High	NS	NS
Brain and other parts of nervous system	High	NS	NS
Lymphosarcoma and reticulosarcoma, etc.	High	NT	NS
Leukemia	High	NT	NS
All malignant neoplasms	Low	NS	NS

[a] Rank 1 is highest rate in group, 6 or 11 lowest.
[b] Two-sided probability (P): NS means not significant. NT means not tested.
[c] From Mason *et al.* (1975). The 95% confidence intervals of local and national rates do not overlap.
[d] National rate outside 95% confidence limits for estimate of a Poisson-distributed variable (Haenszel *et al.*, 1962).
[e] Reference appears to be in error.

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TABLE 6

ANGLO-WHITE MALE CANCER INCIDENCE RATES IN NEW MEXICO, 1969–1974[a]

Neoplasm (ICDA 8)	Los Alamos Co.		Bernalillo Co. (Albuquerque)		New Mexico	
	Cases	Rate	Cases	Rate	Cases	Rate
Stomach (151)	3	28.4	37	8.1	131	8.6
Large intestine (153)	11	60.7[b]	136	30.0	387	25.8
Rectum (154)	3	38.2	69	15.1	175	11.7
Biliary passages and liver (155, 156)	2	5.7	26	6.2	83	5.6
Pancreas (157)	4	29.3	55	12.5	150	10.0
Trachea, bronchus, and lung (162)	5	72.4	325	69.7	977	63.9
Prostate (185)	6	47.2	336	80.7	866	60.0
Bladder (188)	4	61.9	142	32.2	309	20.7
Brain and other parts of nervous system (191, 192)	2	3.7	40	7.7	104	6.4
Lymphosarcoma and reticulosarcoma, etc. (200, 202)	3	6.5	32	6.6	110	7.1
Leukemia (204, 205, 206, 207)	5	12.7	71	15.2	198	13.1
All malignant neoplasms	62	420.2[b]	1739	380.0	4696	311.0

[a] Rates are per 100,000, age-adjusted to U.S. 1970 population. Source is New Mexico Tumor Registry of October, 1976 for years 1969–1974. Rates may be compared to rates based on ICDA-6 classification, although in ICDA-8 neoplasms of the pleura are no longer included with lung, and neoplasms of urachus and urethra are no longer included with bladder.

[b] State rate falls outside 95% confidence interval of this county rate.

the period of excess mortality in males. Current incidence rates in females are elevated, although based on small numbers.

DISCUSSION

Because of public concern over potential health hazards of ionizing radiation, discussion of the preliminary substantive results presented above is warranted. The findings remain consistent with the previous report (Voelz *et al.*, 1978). Analyses of more up-to-date cancer morbidity and mortality data are currently under way.

The major thrust of this paper, however, with respect to this "Workshop on Health Surveillance around Point Sources of Pollution" is in regard to the methodological issues arising during the course of the study. In the main, these issues are not resolved. So following discussion of actual cancer risks in Los Alamos County, we discuss some relevant intervening variables and then some potential approaches to county-based ecological studies of health effects about point sources of pollution.

Cancer among Los Alamos Residents

Preliminary conclusions about cancer in Los Alamos County are considerably strengthened by two factors: (1) the very high correlation of maleness with an

TABLE 7

WHITE FEMALE CANCER MORTALITY AND MORBIDITY IN LOS ALAMOS COUNTY FOR SELECTED SITES[a]

	Mortality rates 1950–1969		Morbidity rates (Anglo) 1969–1974		
	Los Alamos County[b]	United States[c]	Los Alamos County[b]	Bernalillo County	New Mexico[c]
Stomach	13.7 (3)	7.07	9.4 (1)	5.8	6.4
Large intestine	17.5 (5)	16.25	68.4 (8)	41.0	31.2
Rectum	3.8 (3)	4.82	7.2 (1)	15.9	11.4
Trachea, bronchus, and lung	11.1 (5)	6.29	0.0 (0)	23.0	19.3
Lymphosarcoma and reticulosarcoma, etc.	0.7 (1)	3.25	28.9 (3)	8.4	7.0
Leukemia	4.2 (5)	5.74	14.8 (3)	10.5	9.4
All malignant neoplasms	127.3 (63)	130.10	422.7 (81)	371.7	300.9

[a] Average annual age-adjusted rates per 100,000. Sources as for corresponding male rates in preceding tables.

[b] Number of cases in parentheses.

[c] No site-specific rates outside the 95% confidence interval of the corresponding county rates.

occupation in the nuclear industry, while females are much less likely to be employed, or radiation exposed if employed, than males, and (2) cancer morbidity and mortality data spanning a 25-year period, data for the last 5 years being cancer morbidity data from the New Mexico State Tumor Registry. These factors allow at least suggestive separation of occupational from residential risks through: (1) inspection of sex differences, and (2) inspection of temporal consistency as evidence of preexisting versus recently acquired risks.

Only lung cancer, digestive tract cancers, especially of the colon, and leukemia and allied disorders (LAD) are sufficiently frequent to warrant discussion in this preliminary analysis. Discussion of cancers of other sites will be deferred to later publications.

Lung cancer among males was clearly statistically significantly low for the 1950–1969 period. This result is consistent with findings on 224 highly plutonium-burdened male workers (Voelz *et al.*, 1978). During the 1969–1974 period male lung cancer increased (based on five incident cases) to the state level for Anglo males. Females showed a very slight (five observed, about three expected) excess in the 1950–1969 period, and a slight deficit of incident cases (zero observed, about three expected) in the 1969–1974 period. The latter observation, a recent deficit, combined with lack of evidence in the occupationally exposed males, suggests that residential, and very limited occupational, exposures to plutonium have not affected lung cancer rates in Los Alamos females. The slight early excess is best ascribed either to chance or to the smoking habits of the older generation of university-educated women. Among males there is no evidence to date of an excess of lung cancer.

Lung cancer has been cited as a major health hazard resulting from inhalation exposures to plutonium. Deceased, nonoccupationally exposed residents of Los Alamos do have tissue burdens, specifically including lung burdens, of plutonium higher than those found elsewhere in the general population (McInroy *et al.*, 1979). Likewise plutonium in soil and vegetation in portions of Los Alamos County is elevated measurably above background levels due to worldwide fallout (Johnson, 1972).

Deaths due to neoplasms of the reticuloendothelial system, hereafter referred to as leukemia and allied disorders (LAD), were present in borderline excess (SMR 163) in Los Alamos County male residents during 1950–1969. However, incidence rates in males from 1969 to 1974 were not elevated relative to rates in Anglo males in New Mexico. Mortality rates for females during 1950–1969 were low. These observations, if not due to chance, suggest possible effects of occupational exposures prior to employment at Los Alamos or during the early years of the nuclear industry when controls of all hazards, including chemicals in the workplace, were not up to current standards. The lack of excess mortality early among females, and the lack of a current effect among this aging cohort of males, specifically suggest an early occupational effect.

Environmental factors implicated as causal for leukemia have been ionizing radiation and organic solvents, specifically benzene (Kinlen, 1977). Less is known concerning environmental agents responsible for lymphomas. Some evidence exists (Beebe *et al.*, 1978; Matanoski *et al.*, 1975a, b) for an etiologic role of radiation for lymphomas, including multiple myeloma.

At Los Alamos the excess of LAD was composed of small excesses across several tumor types: Hodgkin's, lymphosarcoma, multiple myeloma, and leukemia. This pattern resembles that in the rubber industry where an excess of both leukemia and lymphosarcoma (and possibly Hodgkin's) are thought to be related to solvent, especially benzene, exposure (Goldsmith and Guidotti, 1977). Exposure to solvents and laboratory reagents has been common at Los Alamos. Voelz *et al.* (1979) in a clinical study published occupational exposure histories of 26 plutonium workers: 10 had specifically noted solvent, hydrocarbon, or laboratory reagent exposures and several other subjects were chemists.

Goldsmith and Guidotti (1977) also reported an excess of lymphosarcoma among engineers in California and electrical workers in Washington State, and suggested soldering fumes, actinic radiation, and polychlorinated biphenyls (PCBs) as potential causes. These occupations would be expected to be important in the occupational histories of individuals working at Los Alamos.

Further, military service in the wet tropics has been associated with excess LAD in Australian servicemen (Davies, 1978). This 2.5× excess of LAD in Australian servicemen with overseas and tropical service (mostly wet tropical), relative to LAD rates in servicemen with only temperate Australian service, was consistent across diagnostic categories including leukemias, lymphosarcoma, and multiple myeloma. Malaria, antimalarial drugs, and nitrites in canned meats were factors suggested for further investigation. Persons employed at Los Alamos following World War II had frequently seen service in that war. Some Los Alamos employees, of course, spent time in the South Pacific during test activities.

We are not suggesting that radiation may not have been a factor in LAD inci-

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dence in the 1950–1969 period at Los Alamos, but rather that prior to and during Los Alamos employment some workers could be expected to have been exposed to a variety of hazards of modern technology, including chemical and electrical hazards, each responsible for some excess LAD.

An excess of LAD does not currently appear in males, suggesting that more recent exposures are not inducing a measurable effect. The elevated recent incidence in females in the 1969–1974 period is based on few cases, but should be reconsidered as additional data become available.

Fatal cancers of the stomach, colon, and rectum were significantly infrequent in Los Alamos males in the 1950–1969 time period, but by the 1969–1974 period incidence rates for these cancers had become high relative to New Mexico Anglo rates, significantly so for colon cancer. Incidence rates for digestive tract cancers, at least stomach and colon, were also elevated in Los Alamos females during the 1969–1974 period.

An occupational or environmental explanation of these findings related to the nuclear industry is unlikely, because the Los Alamos females, not occupationally exposed to hazards in the nuclear industry, did not share the low mortality rates of males during the 1950–1969 period. Their rates were quite average.

A reasonable explanation for the observed pattern of rates is that both Los Alamos males and females share underlying high risks of digestive tract cancer, particularly of the colon and rectum, but that these risk factors were counteracted in the first two decades among the males by a healthy worker effect (possibly combined with healthy military and healthy regional migrant effects).

High social class and urban residence are very strong risk factors in colon and rectum cancer (Hoover *et al.*, 1975; Lynch *et al.*, 1975). The risks attached to high social class observed by Hoover *et al.* are consistent with the twofold excess risks observed in Los Alamos residents. Los Alamos County averages among the highest counties in the nation with respect to social class. It is also likely that Los Alamos residents were more urban during early life than the Anglo New Mexico population as a whole.

Males in Los Alamos, however, were almost universally selected for employment in a demanding industry and often for regional geographic mobility. Females in most cases have been subject to selection only by marriage to such males. Healthy worker effects dissipate over decades (McMichael, 1976), as would other similar selective pressures, one assumes.

More extended discussion of general selective factors, employment, migration, ethnicity (white), and military status is desirable, as these are all factors which at Los Alamos or elsewhere, are likely to complicate explanation of observed mortality patterns in small areas.

Miscellaneous Intervening Variables

Employment, ethnicity, military service, and migration may singly or in combination be relevant to the interpretation of disease rates in small areas, including Los Alamos County. We present here only a somewhat arbitrary introduction to the relevant literature.

That employment, which leads to the "healthy worker effect" may be relevant to interpretation of mortality rates in small areas is not immediately obvious. It is discussed here only to emphasize the relevance, and the observation that its effects may be observed into the third decade if our interpretation of lung and colon cancer rates in Los Alamos County is correct. An even stronger effect on cardiovascular mortality in Los Alamos County males exists and will be described in a paper now in preparation.

A "healthy worker effect" may be assumed to be observable in a county or community developing around a new industry or facility. McMichael (1976) and the other authors contributing to the special issue (March 1976) of the *Journal of Occupational Medicine* present exceptionally thorough discussions of the "healthy worker effect."

Ethnicity is most conveniently thought of as two variables, "country of birth" and "national origin, or surname." The latter variable represents an attenuated "country of birth" but could be generally useful across the United States. Surname classification was used by Cook *et al.* (1972) in Ontario. With the development of computerized surname classification programs, and their application to state tumor registry and death certificate files, adjustment for any peculiarities of locally relevant national-origin subgroups could be readily carried out. At least one such program exists.

Until that time, "country of birth" may be relevant to the interpretation of some Northeastern, Northern Midwest, and urban mortality rates. Polish, Italian, and French Canadian subgroups have been studied (Graham *et al.*, 1963; Cook *et al.*, 1972). Haenszel (1961) presented nationwide cancer mortality rates for the foreign born from twelve countries.

It should be noted that the Anglo population of Los Alamos County may not be perfectly comparable with the remainder of the New Mexico Anglo population. There are present not only representatives of the white ethnic subgroups characteristic of the large urban centers of the East and Midwest, but individuals from the Upper Midwest of German and Scandinavian origin.

Some small geographic areas are dominated by military installations; and industrial facilities developed in the decade after World War II, including of course nuclear facilities, may have employee populations made up in considerable part of World War II veterans. Mortality rates within the first few years of discharge were considerably lower than those in the general population. The effect diminished with time but still persists 23 years from discharge. The effect extends to malignant neoplasms. The selection process into the military is held primarily responsible (Seltzer and Jablon, 1974) but the medical services of the Veterans Administration may play a role (Comstock, 1975). The effect varied by rank over the full 23-year period of follow-up, the mortality of privates being very close to expectation, of noncommissioned officers 23% below expected, and of commissioned officers about 40% below expected (Seltzer and Jablon, 1977). The latter might be expected to be overrepresented among veterans in highly technological industries. Ex-prisoners may show excess mortality due to tuberculosis, trauma, and cirrhosis (Keehn, 1980).

We are not aware of quantitative estimates of the percentages of World War II or Korean Conflict veterans among employees of the nuclear industry, but consider that the percentage is likely to be sizeable.

A healthy military effect may well not be additive to a healthy worker effect. It seems likely that they, in fact, represent the same underlying characteristics of the respondents.

Migration must be dichotomized into internal migration and international migration, the latter being dealt with as ethnicity above. Internal migration stands for a set of concepts complex both conceptually and practically.

Internal migration effects are of two types, dilutant and selective. The loss of exposed population or gain of unexposed population in a small study area leads to dilution of expected effects. That people who move may or may not differ from lifetime residents leads to possible selective effects.

Dilution effects are very important in studies of mortality in small areas, but only recently has Polissar (1980) systematically estimated the potential magnitude of these effects in cancer studies. Losses in sensitivity are a function of cancer site, latent period, and the type (size) of geographic units for which rates are calculated (towns, counties, or states). Polissar estimates that at the county level, during a 30-year latent period, 40–50% of relative excess risk may not be reflected in the estimated risk for most cancers. The reader should refer directly to this excellent paper if concerned about internal migration.

Dilution effects around point sources are very likely to occur, since the size and composition of the population immediately surrounding the point source often reflect employment at the source or associated installations and are affected by activation or inactivation of the facility.

Selective effects of internal migration are very poorly known, and one can dissociate them into at least three quite different variables: residential mobility per se, or number and type of moves; class of place specific, rural-to-urban for example; and location specific, carrying the risks associated with a given locale along to a new location. Residential mobility per se is also likely to be a gross oversimplification: distance moved and the type of economic gain anticipated are likely to be very important.

Substantive findings are difficult to locate. Despite an impressive beginning (Haenszel *et al.*, 1962; Haenszel and Taeuber, 1964; Taeuber *et al.*, 1968), studies relating internal migration to cancer mortality do not seem to have progressed. Haenszel *et al.*'s results suggested that individuals living in three or more places had higher lung cancer risks, as did the farm born who migrated to metropolitan areas. Lifetime residents had the lowest risks.

However, in studies of chronic respiratory disease, which is caused by the same variable as lung cancer to a large degree, migration effects have not appeared. Anderson *et al.* (1965) found no relationship of respiratory symptomatology to residential mobility in a British Columbia population. Stebbings (1971) found no relationship of respiratory symptoms in nonsmokers to geographic mobility as estimated by contiguity of place of birth (contiguous counties, contiguous states, other).

The intervening variables discussed above, and many others relating to the levels and causes of mortality in geographically defined populations are given in a recent and lengthy review by Curtiss and Grahn (1980).

The Use of County Data Bases

The study of mortality in small areas has been made easier by the publication of atlases of mortality and compendia of county mortality rates, and by the development of [illegible] computerized data bases incorporating county population, mortality, and socioeconomic data. Methodological and institutional constraints exist, however, which limit the utility of these publications and data bases to the local investigator.

The ultimate need is for a service bureau which can furnish a local investigator not only with the requisite mortality, population, and socioeconomic data, but also epidemiologic and statistical advice concerning the calculation of expected levels of mortality, whether by multivariate adjustment or by selection of control areas, and the calculation of the statistical significance of the findings. In our opinion, further methodological development on these latter two points is required. In this discussion we would like to elaborate slightly on the methodological issues, and review briefly some of the existing data bases, especially some lesser-known ones developed by Department of Energy contractors.

There are three general approaches to the establishment of expected values for a study area: a multivariate analysis of social, economic, and demographic characteristics of a large number of areas as these predict the corresponding mortality rates; careful selection of similar control areas from a regional or national set of areas (the approach utilized in this Los Alamos County study); and utilization of rates of neighboring, contiguous geographic areas. Only the latter technique is readily available to the local investigator with limited computer experience and facilities and limited statistical expertise. Even selection of a number of control counties, by criteria as simple as those utilized in the Los Alamos County study, is extremely tedious done manually, and rather hazardous in the sense that mistakes can easily occur. On the computer, of course, it is easy; especially so if the data base is accessible through a true data base management system (DBMS) such as System 2000.

We have utilized two methods of selecting controls, and also used the state population and population of the largest county within the state as comparison populations, and found the inferences to be drawn from nearly all comparisons to be the same (Tables 4 and 5). This may be a consequence of looking at a truly extreme study area. Some empirical testing of the robustness of conclusions following upon alternative strategies for control selection needs to be done.

The approach to significance testing of the study area against control counties in this Los Alamos study deliberately emphasized the geographic heterogeneity of the control counties selected and did not take into account their population sizes. In this instance the number of control counties was too small for strong inference (although the availability of other tests and the consistency of findings makes this point of little substantive importance in interpreting these Los Alamos findings).

In general, however, the question of whether tests of significance in similar analyses should be based on variance among areas (as done above) or on variance among individuals in the populations (as is most frequently the case), is a question which has not been given the attention it deserves. The common technique of summing age- and sex-specific numerators and denominators across control areas bases the test of significance on variance among individuals. And, given the highly skewed distribution of population sizes in small areas, the composite control area will most often be dominated by one or two specific areas.

The geographic point of view considers that the appropriate test derives from the distribution of all possible comparisons between an area and its proper control(s). This distribution can only be derived empirically. We only raise this issue here: further work in this area is needed.

The preeminent county data base is that of the National Cancer Institute (NCI) relating to cancer mortality. This has been published as county data (Mason and McKay, 1974) and in atlas form (Mason *et al.*, 1975, 1976). A number of substantive publications have derived from this data base. Polissar (1980) cites several of these.

An example of investigations concerning areas of apparent excess risk identified from the NCI data base is the investigation of New Jersey cancer rates by Greenberg *et al.* (1980) which demonstrate that historical trends at the regional and national level must be taken into account. Sauer and Parke (1974) give a useful guide to interpreting extreme county mortality levels from a similar data base.

Similar data bases are being developed elsewhere, as for Canada (Statistics Canada, 1980), and for other diseases, as for cardiovascular and cerebrovascular disease (Fabsitz and Feinleib, 1980). An excellent overview of health-related mapping projects, and of the methodological problems involved is given in the "Proceedings of the 1976 Workshop on Automated Cartography and Epidemiology" (NCHS, 1979).

Not all data bases of use to epidemiologists have been developed under National Institutes of Health auspices. A wide variety of data bases relating to energy, population, environmental quality, economics, and agriculture exist. A useful introduction to these is given by Morris and Novak (1979) who published the proceedings of a computer-based conference on the use of county-level data.

The Department of Energy has funded development of health-related county data bases at Argonne National Laboratory, Brookhaven National Laboratory, and Lawrence Berkeley Laboratory. Samuel Morris of Brookhaven and Susan Sacks representing Lawrence Berkeley each described the data base at their home laboratories at the Workshop on Health Surveillance around Point Sources of Pollution.

A description of the Brookhaven county data base "MEDABA" has been published (Bozzo *et al.*, 1978). MEDABA includes population, net migration of population, 1976 population estimates, energy use and emissions per square mile, and 1969–1971 mortality by cause.

The Lawrence Berkeley Laboratory data base "PARAP" (Populations-at-Risk-to-Air-Pollution) has been described by Merrill *et al.* (1978). The data base contains socioeconomic and demographic data from the 1970 census of population, air quality data for 1974–1976, mortality data for 1968–1972 for 53 causes, and cancer mortality for 1950–1969 combined. This data base is freely 00130021.017e to outside users for government-funded research purposes, and may be accessed using System 2000 commands.

These county data bases are very powerful tools. An administrative structure which will make such data and the required epidemiologic and biostatistical advice available to the novice user is required. It is unrealistic to expect a state epidemiologist, a county health officer, a union industrial hygienist, or a corporate medical director to be able to use such a tool adequately. A service needs to be provided.

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