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

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Abstract

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

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

1. Introduction

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

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

2. Methods

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

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

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

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

2.2. Cancers considered in the study

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

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



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

2.3. Mortality data

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

2.4. Study county (figure 1)

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

2.5. Control counties

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

County	Total popul- ation 1990		Percentages (%)										
		Male	White	Black	Hispanic	Rural	>64 y	Below poverty	High school graduate	Employed	household income (\$10,000)		
					Sti	udy cou	nty						
Karnes	12 455	48	97	3	47	46	16	36	51	50	16.2		
					Con	trol cou	nties						
DeWitt	18 840	47	89	11	24	53	19	25	55	49	18.0		
Frio	13 472	49	98	1	72	29	10	38	50	53	14.1		
Goliad	5980	48	93	7	36	100	16	18	63	53	21.4		
La Salle	5 2 5 4	50	99	0	75	29	14	37	45	51	15.6		
					А	All contr	ol						
	43 546	48	93	6	47	49	15	29	56	51	18.5		

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

2.6. Statistical analyses

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

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

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

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

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

3. Results

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

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

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

	1950–2001, in Karnes County and in the four control counties. ('Obs' stands for 'Observed'.)											
	Calendar years of death											
	1950–64		1965–79		1980–89		1990–2001		All			
	Obs	SMR ^a	Obs	SMR ^a	Obs	SMR ^a	Obs	SMR ^a	Obs	SMR ^a		
Karnes County	267	0.9 ^c	331	0.9 ^c	279	0.9	346	0.9 ^c	1223	0.88 ^c		
Control counties	799	0.8 ^c	1102	0.9 ^c	818	0.8 ^c	1138	0.9 ^c	3857	0.88 ^c		
RR ^b	1.0		0.9		1.1		1.0		1	1.0		

Table 3. Mortality due to all types of cancer, all ages and sexes combined over four time periods,

^a SMR is the observed number of cancers divided by that expected based on rates within the general population of the United States.

^b Estimated RR taken as the ratio of the SMR in Karnes County with that in the four control counties.

^c p < 0.05.

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

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

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

4. Discussion

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

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

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

^a p < 0.05.

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

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

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

Reports of small clusters of childhood leukemia around nuclear installations in the United Kingdom in the 1980s prompted several large scale systematic surveys around the world (UNSCEAR 1994). Subsequent surveys in other counties failed to confirm a link between childhood leukemia or any other cancer and proximity to nuclear installations (Doll et al 1994, Doll 1999). Several geographical correlation studies around nuclear installations in Spain have been published recently suggesting an increase in cancer mortality in areas containing uranium processing facilities, including one that also contained a nuclear waste storage facility, but not in areas with nuclear power plants (López-Abente et al 1999, 2001). However, the cancer mortality rates in the towns near the uranium operations were below expectation based on general population rates (SMR 0.88) and it was the even lower rates among the more distant towns (50–100 km) used as control that produced the apparent elevation. The areas with uranium facilities, then, did not experience elevated cancer rates but rather the control areas experienced unusually low cancer rates. This suggests that the residents of the control areas may not have been similar to the residents of towns near uranium processing facilities and such non-comparability tempers interpretation (Laurier et al 2002). Further, cancer risks overall and for lung cancer and kidney cancer in particular were lower in the towns nearest (<15 km) to the uranium facilities than in the towns located further away (15–30 km), which is just the opposite to what would be expected if radiation were a contributing factor. In addition, the elevated mortality rates were gender specific in that lung cancer increases were seen only in males and not females, whereas kidney cancer increases were seen only in females and not males. Such differences are also not consistent with a possible effect of environmental exposures, because any exposures common to both sexes would be expected to affect both males and females and not just one or the other. Similarly, a slight increase in leukemia reported in the Spanish study (López-Abente *et al* 1999) is not in accord with what is known about the distribution of uranium in the body after intake, i.e., exposure to the leukemia-producing cells is minuscule (Bender *et al* 1988, Priest 1989). Further a radiation link between leukemia and living near nuclear installations has been discounted after extensive epidemiologic study (UNSCEAR 1994, Laurier *et al* 2002). Finally, uranium processing facilities in the US have not been correlated with increased cancer mortality (Jablon *et al* 1990, Boice *et al* 2003a) or cancer incidence in nearby populations (Boice *et al* 2003b). Thus the exploratory correlation studies in Spain must be interpreted with caution, since the mortality excesses and deficits may be attributable to bias if control area residents were not comparable to study area residents in terms of cancer risk factors or, as mentioned by the authors, to chance when so many hundreds of comparisons are made (11 different cancers, 8 installations and 3 distances).

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

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

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

4.1. Strengths and limitations

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

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

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

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

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

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

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

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

5. Conclusions

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

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

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Résumé

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

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

Zusammenfassung

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

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