Epidemiology Study Evaluation Matrix on
Mangano, J., Cancer Mortality near Oak Ridge, Tennessee.
The International Journal of Health Services <u>24</u>:521-533, 1994.

Evaluation Questions	Report Statement	PHAWG Discussion	PHAWG Finding
1a.) Why was this study done?	To determine "whether substantial amounts of radiation have had an effect on cancer death rates."	To examine cancer mortality from low-level radiation among 94 counties within a 100-mile radius of Oak Ridge Reservation.	Purpose as stated in the report is reasonable.
1b.) What hypothesis is the author testing?	Tested five hypotheses to determine whether substantial amounts of radiation in the Oak Ridge areas have an effect on cancer death rates. p.524	Hypotheses: 1. The increase in the cancer mortality rate near Oak Ridge should exceed the national and regional increases. 2. Within the Oak Ridge region, the increase in the cancer mortality rate should be greatest in rural areas. 3. Within the Oak Ridge region, the increase in the cancer mortality rate should be greatest near the weapons plant. 4. Within the Oak Ridge region, the increase in cancer mortality rates should be greatest in mountainous areas. 5. Within the Oak Ridge region, the increases in the cancer mortality rate should be greatest in the area downwind of the weapons plant.	Hypotheses are stated clearly.
2. What type of study was this?	Author does not state the type of study.	Both descriptive and analytic characteristics.	Primarily a descriptive study with analytic characteristics/ components.
3a.) Who was the study population?	Whites within "the 94 counties that are completely or mostly situated within 100 miles of Oak Ridge, plus nine other nearby counties included in analysis of the fourth hypothesis". The 94 counties are located in five states: 46 in Tennessee, 19 in Kentucky, 16 in Georgia, 11 in North Carolina, and 2 in Virginia. p.525	White people who died from cancer and were living within the 94 counties that are within in a 100-mile radius of Oak Ridge during two time periods (1950–1952 and 1987–1989).	Author clearly defined population under study.

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3b.) There were five sub-groups; one for each hypothesis.	Each hypothesis also had its own specific population: 1. People living within the 94 counties within 100 miles. 2. Rural compared to urban populations. 3. People living within Anderson County compared to those living in the other 12 counties within 40 miles. 4. Mountain compared to lowland populations. 5. Upwind compared to downwind populations.	Five sub-groups identified correspond to hypotheses being tested.	Author defined sub-groups for each hypothesis.
4. What was the exposure of interest?	Low levels of radiation from "Radioactive chemicals routinely released from nuclear facilities into the environment primarily reach the general population through the food chain." p521, 522 The author specifically mentions iodine-131, strontium-89, strontium-90, cesium-137, and cobalt-60 released into the soil, water, and air. p.522-23	Chronic ingestion of substantial amounts of low-level radiation.	PHAWG concluded that chronic ingestion of low-level radioactive material was the exposure of interest.
5a.) How was exposure defined and measured?	Exposure was defined in general as the Oak Ridge area.	Exposure was not measured, but it was defined as living in 94 counties within 100 miles from Oak Ridge, rural areas, close to Oak Ridge, mountainous areas, or downwind.	PHAWG decided that exposure was not measured, but was defined as living in 94 counties within 100 miles from Oak Ridge, rural areas close to Oak Ridge, mountainous or downwind areas.

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5b.) What is the type of exposure classification.	Each hypothesis has a specific definition of exposure. 1. 94 counties nearest OR. 2. Rural areas (nonurban) counties near OR. 3. Anderson county where the Oak Ridge nuclear facilities are located. 4. Mountainous counties near Oak Ridge. 5. Downwind counties under 40 miles from OR.	Types of exposure classifications used were generally considered poor in the hierarchy provided in the worksheet. The following types of exposure classifications were used: 1. Residence in a defined geographical area (e.g., county) of a site. 2. Residence in a geographical area in proximity to a site where exposure is assumed. 3. Distance or duration of residence (duration was not measured).	PHAWG decided that exposure classifications were based on: 1. Residence in a defined geographic area (e.g., counties in proximity to a site). 2. Residence in a geographic area in proximity to the site where exposure is assumed. 3. Distance and duration.
5c.) What are some limitations or criticisms on how exposure was measured in the study.	Author cited reports of estimated releases of radioactive products from the Oak Ridge facilities. Author stated the following limitation of measuring exposure: 1. "Accurately measuring the amount of internal-organ doses received by the general population is impossible. Thus, there is no way of precisely knowing the radiation intake of each Oak Ridge area resident in the past 50 years." p.522 "Even without knowing exact amounts of radiation added to the Oak Ridge area environment and how much was ingested by residents" he could test the five hypotheses." p.524	Limitations: - Exposure was not measured; Mangano quantified releases in the study, but not exposures. - Just because you died of cancer according to your death certificate, does not mean you were exposed to low-level radiation. - Streams and tributaries downstream from Oak Ridge were not evaluated as a pathway. - There was no consideration of underground water pathways. - There are a lot of other differences between the 1950 and 1980 populations that could account for the increase in cancer rate. - Not all cancers are known to be caused by radiation.	PHAWG decided that exposure was poorly defined and not measured. Duration was not measured. In addition, PHAWG decided that these types of exposure classifications were considered poor in the exposure hierarchy (with residence in a geographic area being the poorest and quantified personal measurement being the best).
6. What was the health outcome of interest?	Changes in cancer mortality rate among whites.	Death rates from cancer in whites.	Author stated outcomes
7. How was the health outcome defined and measured in the study?	Health outcome was defined as "death rates for all cancers (total)" and measured using National Cancer Institute death rates. p.525	Vital statistics data from the National Cancer Institute for the populations identified in the five hypotheses.	The cancer death rates were obtained from data from the National Cancer Institute.

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8. Could there have been bias (distortions or error) in how study subjects got selected into the study?	The author did not identify any bias in the selection of study subjects.	This question does not apply to this study because subjects were not chosen.	PHAWG decided that this question was not applicable because the subjects were not selected in this study.
9. Could there have been bias (distortions or error) in how information was collected from the study group and comparison group?	The author did not identify any bias in how the data were collected.	The early years may actually have a higher rate of death from cancer than reported because cancer may not have been identified as the actual cause of death in the 1950s and there was a better ability to diagnose cancer in the 1980s. Therefore, the difference observed between the 1950s to the 1980s may be exaggerated. In the 94 counties, and the Southeastern U.S. in general, cancer rates may be lowered by the fact that overall life expectancy is lower—thereby reducing the number of people who will live long enough to die of cancer. There were significant changes in population between the 1950s and 1980s because of the war and plant construction (e.g., there was a large influx of people into Anderson County in 1948 and a rapid decline after construction was complete and the war ended). The result of these changes was that there was a larger population of young people, who are not likely to have cancer, in the 1950s than there was in the 1980s. PHAWG questioned the ways in which the proximity of counties to Oak Ridge and to each other were determined. For example, three Oak Ridge plants are located in Roane County, but Roane County is considered to be further away from Oak Ridge than Anderson County.	PHAWG determined that there are several potential sources of bias, distortion, or error in the death certificate data but not in the collection of the data by the author. PHAWG also concluded that the proximity of the plants to the counties is inaccurate. PHAWG determined that there was an error in selecting counties nearest the weapons plant. Two of the three facilities are located in Roane County but Roane County was not included in the study group nearest the site. The criteria for selecting the study group exempted urban counties, but the comparison group includes both rural and urban counties.

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10. Could the results have been due to confounding? What are potential confounders in this study?	The author stated that "A brief review of demographic data revels no other apparent reason for this distinct and consistent set of trends." p. 531	Mangano's study assumed that the comparison group is not exposed to any natural or background sources of radiation. The National Cancer Institute highlights a similar trend of increase in cancer throughout the entire Southeast and East, which would not be attributable to Oak Ridge. In the 1980s, people were more exposed to carcinogenic compounds because of use of self-service stations, rather than the full-service stations that were used in the 1950s. Relatively high utilization of pesticides in rural areas (as opposed to urban areas) might be confounded with the hypothetically greater exposure to Oak Ridge pollutants among rural residents. The smoking of unfiltered cigarettes and the use of chewing tobacco is more prevalent in the southeastern United States than elsewhere in that country. Both coal mining and coal consumption were higher in the 1950s than they were in the 1980s. This fact may partially or completely explain the change in cancer incidence reported for the northwest counties. Health care and diagnostic ability improved with time. Alcohol consumption might confound the results.	PHAWG concluded that there were a number of confounders that were not addressed in the study: 1. Coal-burning power plants in the region operated by TVA, 2. Occupational exposures associated with coal mining, 3. Use of chlorine in drinking water, 4. Smoking 5. Use of pesticides by regional farmers, 6. Natural background radiation, and 7. Availability and sophistication of medical care between the two time periods under consideration.

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11. Describe the methods used to measure the relationship between exposure and disease?	"Comparisons were made using rates (age adjusted to the 1950 standard) for the period 1950-1952 and 1987-1989." p.525 1. The increase in age-adjusted cancer mortality rate for whites in the 94 counties between 1950–1952 and 1987–1989 was compared to the increase in age-adjusted cancer mortality rate for whites nationally and the southeast regional between 1950–1952 and 1987–1989. 2. The increase in cancer mortality rates for whites in the nonurban counties between 1950–1952 and 1987–1989 was compared to the increase in cancer mortality rates for whites in the urban counties between 1950-1952 and 1987-1989. 3. The increase in cancer mortality rates for whites in Anderson County between 1950–1952 and 1987–1989 was compared to the increase in cancer mortality rates for whites in the 12 counties less than 40 miles away between 1950-1952 and 1987-1989. 4. The increase in cancer mortality rates for whites in the mountainous counties between 1950–1952 and 1987–1989 was compared to the increase in cancer mortality rates for whites in the lowland counties between 1950-1952 and 1987-1989. 5. The increase in cancer mortality rates for whites in downwind counties between 1950–1952 and 1987–1989 was compared to the increase in cancer mortality rates for whites in the upwind counties between 1950-1952 and 1987-1989.	The method used for age adjustment was the direct method. The author did not examine age-specific cancer death rates.	PHAWG decided that the direct method of age adjustment may not be the best method.

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12. What are the major results of this study?	1. The cancer mortality rate for whites in the 94 counties increased by 34.1% between 1950–1952 and 1987–1989, compared to an increase of 5.1% for whites nationally. This difference in the percent increase was statistically significant. The 94 counties rate, which was considerably below the corresponding U.S. rate in 1950–1952, rose to a rate just exceeding the national rate in 1987–1989. During 1950–1952 the 94 counties age-adjusted cancer mortality rate for whites was 111.6, in comparison to 139 for the U.S. rate. During 1987–1989, the Oak Ridge area age-adjusted cancer mortality rate climbed to 149.7, in comparison to 146.3 for the U.S. rate. The Oak Ridge area increase of 34.1% was also significantly (statistically) higher than the southeast regional increase of 28.2% between 1950–1952 and 1978–1989. 2. The change in cancer mortality rates between 1950–1952 and 1987–1989 in the nonurban counties (39%) was higher than the corresponding change in cancer mortality rates of the urban counties (22.9%). This difference was statistically significant. Although the urban rate was considerably higher 40 years ago (121.7 in comparison to 107.8 for nonurban counties during 1950–1952), by 1987–1989 the rates in the two categories were nearly identical (149.4 for the urban counties and 148.9 for the nonurban counties).	Hypothesis 1: The difference in cancer rate between the 1950s and 1980s may have been exaggerated because (1) cancer may not have been diagnosed as the cause of death in the 1950s and there was a better ability to diagnose cancer in the 1980s, (2) cancer rates fluctuate from year to year around an average and a change in a few years before or after 1950-1952 may have made a difference in the cancer rate, and (3) the younger age of the working population in the 1950s would result in a lower cancer rate for the population. Hypothesis 2: Variation in doctor care between rural and urban areas could have affected the ability of the doctor to accurately diagnose the actual cause of death. [In addition, the counties designated as urban, geographically had large rural areas in the 1950s]. Hypothesis 3: There was a question on how proximity to Oak Ridge was determined. Three plant sites are located in Roane County, yet Roane County is considered to be farther away from Oak Ridge than Anderson County. The study compared the cancer rates of Anderson County with that of 12 counties within 40 miles from the site; the difference between the rates was not statistically significant. The study also showed that the cancer rate for Anderson county was 39.1%, which is closest to the Oak Ridge site, and the cancer rate for Anderson, Campbell, and Union counties combined was 50.8% indicating that the cancer rates for Campbell and Union counties, which are farther from the Oak Ridge site, had to be much higher than that of Anderson County for the three counties combined to exceed that of Anderson	PHAWG agreed that the author presented the results of the study in the report. (The author's results are contained in column 2.)

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12. What are the major results of this study? (cont.)	3. Between 1950–1952 and 1987–1989 the cancer mortality rate increased 39.1% in Anderson County, the county nearest the reservation, in comparison to 29.5% in the 12 counties less than 40 miles away. This difference was not statistically significant. 4. The cancer rate increased 40.4% between 1950–1952 and 1987–1989 in the mountainous areas of Oak Ridge in comparison to 30.3% in the lowland regions. This difference was statistically significant. In 4 of 5 matched pairs (mountainous areas with equidistant lowland areas), the percent rate changes were higher in the mountainous areas. The greatest percent change from 1950–1952 to 1987–1989 between mountain and lowland areas occurred in the two pairs closest to Oak Ridge. 5. The increase in cancer death rates between 1950–1952 and 1987–1989 in the three downwind counties northeast of Oak Ridge (Anderson, Campbell, and Union) was 50.8%. In comparison, the increase in cancer death rates in the upwind counties southwest of Oak Ridge (McMinn, Meigs, Rhea, and Roane) increased 7.1% and the increase in cancer death rates in northwest counties and southeast counties was 88.2% and 19.5%, respectively.	Hypothesis 5: The dose-reconstruction study noted that at elevations >500 meters, the wind direction is southwest to northeast, but in the valleys the wind blows equally in both directions. The largest increase in cancer rates was in the northwest, which is not downwind of Oak Ridge. [The northwest area which is neither downwind nor upwind of Oak Ridge had the largest increase in cancer rate. Mangano explained this increase by noting that these counties are in mountainous areas. However, if the mountainous areas with the largest increase in cancer rate is not downwind to Oak Ridge, then it is doubtful that radioactive products from Oak Ridge are transported to these areas where they are washed out by the rainfall and enter the food chain]. In summary, Mangano concluded that the cancer mortality rate increase in the Oak Ridge area exceeded the national and regional increases; the local urban areas experienced less of an increase; the change was greatest in the area closest to Oak Ridge; increases in mountain areas surpass those in adjacent lowlands; and the increase was greatest in the area downwind of Oak Ridge.	

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12. What are the major results of this study? (cont.)	The 1950–1952 downwind counties age-adjusted cancer mortality rate for whites was 105.0, which is considerably lower than the corresponding 1950–1952 upwind counties rate of 138.2. The 1987–1989 downwind counties age-adjusted cancer mortality rate of 158.3 is slightly greater than the corresponding 1987–1989 upwind counties rate of 148.0 and less than northwest counties rate of 177.1.		
13. Do you believe the results of the study? Were the results valid?	"Each of the five hypotheses was supported by the data presented here." P.530	PHAWG does not believe that Mangano's analyses and results support his conclusions.	PHAWG concluded that the analysis and results of the study did not support the author's conclusions due to the following: 1. Failure to measure or estimate radiation exposure for the selected population. 2. Failure to address other known sources of contamination and/or confounders. 3. Failure to support key exposure assumptions with data or citations. 4. Failure to address the northwest counties with the highest increases in cancer death rates.
14. What is the potential impact of the study on public health practice or on future research in the area?	"In conclusion, the study strongly indicates that current U.S. policy and existing radiation standards for environmental releases must be reevaluated. Substantial evidence is building against the belief that routine, low-level releases form nuclear weapons plants and civilian nuclear reactors are not harmful."	PHAWG did not discuss this question.	