Short report

A note on "Job related mortality risks of Hanford workers and their relation to cancer effects of measured doses of external radiation"

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Although it is not our intention to provide a complete critique of the latest analyses of the Hanford data by Kneale *et al.*,¹ we wish to comment briefly and to present some results of our own analyses of the Hanford data for comparison. In an earlier paper of Kneale *et al.*² internal monitoring levels played a key part as a control variable. In the latest paper¹ this variable has been replaced with a measure of job hazard developed by the same authors in a companion paper.³ We will not comment on the construction of this variable, but we do wish to note that the results of analyses using this new variable clearly differ from those in the earlier paper. The *t* value for the analysis of cancers of radiosensitive tissues (A-series) with control for job hazard and other "obvious" factors based on untransformed doses and no allowance for cancer latency or exposure age (table 9¹) is 0.77. This may be compared with a *t* value of 2.47 for a comparable analysis presented in the earlier paper (using internal monitoring levels instead of job hazard). Kneale *et al.* do not comment on the implications of this change, but it is clear that the strength of the association of cancer mortality and exposure to radiation has been weakened with the use of the job hazard variable and the inclusion of recent deaths. No estimates of radiation risks are offered in the most recent paper, but they would probably differ substantially from those presented earlier.

Kneale *et al.* obtain statistically significant results only by analysing ranks instead of doses, or by allowing for an age effect as well as by restricting the analyses to a subgroup of cancers identified as cancers of radiosensitive tissues (A-series). The use of

ranks (which in this application is similar to analysing the logarithms of doses) involves searching for the measure of dose that correlates best with A-series cancer mortality. Since there is no a priori reason (based on data from populations other than Hanford workers) to think that the dose response curve will be logarithmic, results of the *t* test presented must be interpreted with caution. In fact, if a parameter describing the shape of the dose response curve had been estimated by maximising the log likelihood an additional degree of freedom would be needed in assessing the statistical significance of the result—that is, a higher value than those attained would be required to achieve statistical significance.

With regard to the age at exposure adjustment, studies of the Japanese A-bomb survivors⁴ and other populations⁵ suggest that relative risks decrease rather than increase with increasing age at exposure. Since there is no a priori justification for the adjustment applied by Kneale *et al.* in table 11,¹ it is again inappropriate to evaluate statistical significance using a simple *t* test. There is, however, an additional problem with the adjustment for age. Kneale *et al.* have controlled for age by using fairly broad age at hire groups (<25, 25–34, 35–44, 45–54, and >55). The age at exposure adjustment consists of "increasing dose by 10% for each year after age 40" with the result that those at the upper end of the 10 year age intervals have their doses increased by more than those at the lower end. Since spontaneous rates for cancer increase appreciably with age, those at the upper ends of intervals also have higher death rates than those at the lower end. The result is a spurious correlation of cancer mortality and exposure that accounts at least in part for the increased correlation produced by the adjustment for age at exposure.

We present here some results of our own analyses of the Hanford data. Our data base is similar to that analysed by Kneale *et al*, but there are some differences, especially for mortality data in recent years when our ascertainment of deaths and certificates has been conducted independently of Kneale *et al*. Ascertainment of deaths for our analyses is based on information provided by the Social Security Administration (up to September 1983), the US National Death Index, the Washington State Occupational Mortality Surveillance System, and the California (State) Automated Mortality Linkage System. Cause of death coding for all deaths was validated by the US National Center for Health Statistics staff in 1983.

The fact that the two data sets are reasonably comparable is shown in table 1. Because we do not yet have certificates for over 20% of the deaths occurring in 1979 and 1980 (fewer than 2% of the certificates are missing for deaths occurring earlier), we have presented deaths both up to 1 January 1979 and up to 1 January 1981 (only deaths with certificates are presented). Kneale *et al* indicate that their analyses include deaths up to March 1980; we are given no information on the completeness of their mortality data, or the procedures used to obtain it.

Because of the possibility of bias resulting from incomplete ascertainment (those deaths without certificates show evidence of a negative correlation with radiation exposure), the analyses presented in table 2 include only deaths up to 1 January 1979. The general method used in conducting these analyses is similar to that used by Kneale *et al*, and has been described by Gilbert⁶ and by Gilbert and Marks.⁷ Our analyses were controlled for single years of age (age plays the part of follow up period in the Kneale *et al* analyses), calendar year (five year intervals except for 1975–8 when single year intervals were used to account for possible delays in mortality ascertainment), sex, and duration of employment (less than two years, and two or more years). Exposures were lagged for a 10 year period as in the results presented in tables 10 and 11 of Kneale *et al*.¹ The A-series cancer group is that specified in Kneale *et al*²—namely, ICD codes 146–159, 162–163, 174, 193, 200–209. We have analysed the A- and B-series separately for the purpose of comparing results, not because we believe that this represents an appropriate grouping. The trend test statistics may be compared with a standard normal distribution to assess statistical significance.

There is no evidence of a negative correlation with exposure for all causes of death, although a negative correlation was found (trend test statistic = 1.77) when the data were analysed with no allow-

Table 1 Number of certified deaths by exposure category at death. (Number of deaths due to cancer given in parentheses)

Dose (rem)	Kneale <i>et al</i>	Our files to 1 January 1979	Our files to 1 January 1981
0-00	1060 (208)	998 (209)	1068 (229)
0-01–	555 (109)	522 (107)	565 (115)
0-08–	869 (164)	819 (154)	878 (174)
0-32–	647 (146)	600 (135)	671 (156)
0-64–	689 (147)	652 (143)	711 (158)
1-28–	530 (115)	491 (109)	551 (121)
2-56–	231 (60)	218 (55)	243 (64)
5-12–	150 (35)	143 (32)	164 (40)
10-24–	96 (23)	92 (22)	107 (26)
>20-48	112 (26)	100 (25)	126 (30)

ance for latency (comparable with the analyses presented in table 6 of Kneale *et al*). At least a part of the explanation for the negative correlation observed with no allowance for latency is that in many cases workers who die will have been ill for some period preceding their deaths, and thus will not be reporting for work and having their dosimeters read. This source of bias will be reduced when the last 10 years of dose is discarded as in the analyses in table 2. The fact that our control variables differ from the “obvious” factors used by Kneale *et al* may also be a factor in the reduction of the negative correlation reported by these investigators. Although the possibility of exposure related bias can never be ruled out in an epidemiological study, there is no strong evidence of such bias in our data for either cancer or all cause mortality.

Table 2 Observed and expected deaths for all certified deaths, A-series (“radiosensitive”) cancers, and B-series cancers with allowance for 10-year latency

Dose (rem)	All certified deaths	A-series cancers	B-series cancers
	Obs/Exp*	Obs/Exp*	Obs/Exp*
0-00	870/835.5	123/125.0	63/49.2
0-01–	499/493.4	79/75.5	21/29.1
0-08–	783/777.0	117/119.1	43/45.8
0-32–	617/593.7	94/89.1	29/35.3
0-64–	533/570.2	84/87.9	38/35.0
1-28–	307/331.0	48/55.6	23/20.5
2-56–	142/149.3	31/25.7	9/9.4
5-12–	93/91.9	16/16.4	5/5.9
10-24–	65/65.7	15/11.4	4/4.4
20-48–	33/34.2	5/6.2	2/2.4
Trend test statistic	–0.67	0.28	–0.43
Probability of trend arising due to chance†	0.75	0.39	0.67

*Expected deaths are calculated from experience of all monitored workers (including survivors) allowing for age, calendar year, sex, and duration of employment.

†Significance levels are for a one tailed test and are calculated using a normal approximation.

The results in table 2 show little evidence of a positive correlation of A-series cancers with radiation exposure. Repeat analyses with ranks (trend test statistic = 0.16) and with the 1979–80 deaths included (trend test statistic = –0.07) also failed to yield significant correlations. There is no evidence of a significant negative correlation for the B-series cancers.

Because of the limited power of statistical tests based on data on Hanford workers, the possibility of radiation induced cancer in the Hanford population cannot be ruled out. Nevertheless, in view of the results presented in the latest paper of Kneale *et al* and our own analyses there does not seem to be any compelling reason to believe that the Hanford data are inconsistent with current estimates of radiation risks.

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References

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