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

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ABSTRACT This paper continues the series by Mancuso, Stewart, and Kneale (MSK) on studies of cancer risks for radiation workers at Hanford. It concentrates on the statistical problems posed by the need to estimate and control for job related mortality risks when there are several changes of occupation and no certainty about how different occupations are related to two socioeconomic factors which have strong health associations—namely, education and income. The final conclusion is that for tissues which are sensitive to cancer induced by radiation there is a risk of cancer for Hanford exposures whose dose response is curvilinear with long latency and increasing effect with increasing exposure age.

Analyses of Hanford data by Mancuso, Stewart, and Kneale (MSK) have aroused much controversy by insisting that the risk of cancer per unit dose of radiation is significantly higher than ICRP 26 recommendations.[1-5] Other investigators have reported negative findings for Hanford workers.[6-8] Mancuso et al, however, are insisting that this is merely the result of using an inappropriate classification of the deaths from cancer, and that it needs only a regrouping of the deaths according to ICRP publication 14[9] to bring all supposedly negative findings into line with MSK findings for cancers of radiosensitive tissues (table 1).

According to MSK these (A) cancers have a significantly high dose compared with non-cancer deaths and a residual group of (B) cancers have a significantly low dose. These are genuine differences since they remain even after control for a wide range of factors in a Mantel-Haenszel analysis,[24] and are also a feature of other analyses of Hanford data (see table 1). Furthermore, the radiation dose for (A) cancers is significantly lower than the dose for survivors, and this difference remained until four levels of radiation monitoring of individual workers were added to the usual controlling factors.[4]

More recent work has shown that the monitoring data for individual workers can be used to separate

safe from dangerous occupations (table 2), and census code numbers (attached to each job title) can be

Table 1 *Effect of reclassifying the cancers included in the analysis of Hanford data by Hutchison et al*

ref (7)

Dose level (rads)	Deaths		Ratio O:E
	Observed	Expected	
All cancers (ICD Nos 180–209)			
0·01–	121	145·7	0·83
0·25–	126	112·0	1·13
0·65–	59	54·8	1·08
1·05–	99	96·7	1·02
4·05–	24	22·1	1·09
>10·05	20	17·5	1·14
Total	449	449·0	—
All cancers of radiosensitive tissue *(ICD Nos 151, 153, 157, 162, 163, 200–209)			
0·01–	72	91·2	0·79
0·25–	77	69·9	1·10
0·65–	35	34·6	1·01
1·05–	67	62·4	1·07
4·05–	18	14·4	1·24
>10·05	15	11·4	1·32
Total	284	284·0	—
Other cancers (ICD Nos 140–149, 154–156, 185–199)			
0·01–	49	54·7	0·90
0·25–	49	42·1	1·16
0·65–	24	20·2	1·19
1·05–	32	34·3	0·93
4·05–	6	7·7	0·78
>10·05	5	6·1	0·82
Total	165	165·1	—

See ICRP 14.

Table 2 *Hanford occupations: types of radiation monitoring and methods of scoring for individuals and occupations*

Danger levels	Types of monitoring	Annual monitoring score	
		Individual workers	Occupations*
1	Film badge only	1	1·0–2·4
2	Film badge and routine urine tests	2	2·5–2·8
3	Repeat urine tests	3	2·9–3·0
4	Repeat urine tests and whole body counts	4	3·1–4·0

*Average monitoring score for all workers representing a given occupation in a given year.

Table 3 *Radiation doses and mortality risks for Hanford occupations and later years.*

Hanford occupations	Danger levels	Man-Years	Monitoring scores* (means)	Measured doses of external radiation ΣMan Rems	Differential mortality scores†
Professional and	1	26 861	1·92	2342	− 228
technical	2	27 208	2·74	4568	− 210
	3	25 584	3·08	6642	− 222
	4	23 754	3·69	15181	− 29
Clerical	1	47 598	2·03	1742	+ 92
Operatives and	1	34 529	2·28	2089	+ 65
other manual	2	27 001	2·76	3394	+ 82
	3	23 167	3·20	3839	− 43
	4	33 828	3·60	28118	− 35
Not recorded	—	19 825	2·56	2369	− 31
Post Hanford	—	661 165	—	0	+ 18
Total	—	950 520	—	70284	0

*See table 2:
†These indices of general mortality measure the change in logit probability ($\times 10^4$) of the annual death rate being higher (+) or lower (−) than the average for all workers (with control for age, sex, and calendar year).

used to separate work which requires professional or technical qualifications from lower grades of work, also clerical from non-clerical work.[10] By combining the occupational monitoring data, over 8000 job titles were eventually fitted into nine occupational groups preparatory to obtaining exact estimates of job related mortality risks.

The statistical theory behind this exact method is described in the appendix. The aim is to measure the differential mortality for each occupational group in such a way that the total score is a suitable controlling factor and the differential mortality component of the score can be estimated efficiently. In practice there is no difficulty provided the total score is defined as the difference between logit mortality rate of a worker at a given age and the logit mortality rate of all workers of similar age, sex, and birth cohort (table 3).

Application of the new controlling factor

The data relating to 21 880 male and 6082 female workers were first divided into 80 cohorts by cross classification of four obvious factors—namely: sex (two levels), hire age (five levels), hire dates (four levels), and duration of employment (two levels). The 80 cohorts and nine occupational groups were then used to estimate job related mortality risks by the method described in the appendix. Finally, five levels of differential mortality for each job title were defined and added to the obvious controlling factors to produce 400 instead of 80 cohorts. As individuals grow older their position on any differential mortality scale is bound to change. Therefore, some Hanford workers may have changed cohorts as they progressed either from hire to death (non-survivors) or from hire to the end of the follow up period (survivors). Nevertheless, this did not prevent each of the 400 cohorts being analysed by the Cox method of regression models in life tables.[11]

Results of present analyses

Before giving the results in their final form it may be as well to present a simple intuitive analysis to convince those who might doubt the need for complicated statistical analyses that the higher doses for survivors than non-survivors does constitute a real

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On. 30902—D83:9—F015—Location G1 Art: Kneale (54)
01—GGS—18.8.83; 04—GS—24.8.83

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01—GGS—18.8.83; 04—GS—24.8.83

Table 4 *First example of a Hanford work cohort: Men hired in 1945 (25–34 years) who worked for less than four years*

Dose (rems)	State in 1955		State in 1965	
	Whole cohort	Deaths after 1955	Whole cohort	Deaths after 1965
0·00–	191	41	177	27
0·01–0·07	73	19	68	14
0·08–0·31	123	24	118	19
0·32–	145	23	135	13
0·64–	164	25	159	20
1·28–	101	15	97	11
2·56–	9	0	9	0
5·12–	0	0	0	0
10·24–	0	0	0	0
>20·48	0	0	0	0
Total	806	147	763	104
Mean dose	0·560	0·440	0·569	0·456

Table 5 *Second example of a Hanford work cohort: Men hired in 1945 (45–54 years) who worked for less than four years*

Dose (rems)	State in 1955		State in 1965	
	Whole cohort	Deaths after 1955	Whole cohort	Deaths after 1965
0·00	24	21	15	12
0·01–0·07	22	15	12	6
0·08–0·31	175	58	36	25
0·32–	122	93	85	57
0·64–	83	57	71	41
1·28–	40	30	36	24
2·56–	16	11	10	8
5·12–	6	3	8	4
10·24–	0	0	7	4
>20·48	0	0	3	1
Total	388	288	283	182
Mean dose	0·817	0·761	1·613	1·403

Table 6 *Comparing all deaths with survivors after control for obvious factors only**

Dose (rems)	Observed	Expected†	t-value
0.00	1060	959·0	+4·03
0·01–0·07	555	561·8	−0·32
0·08–0·31	869	829·2	+1·58
0·32–	647	650·1	−0·14
0·64–	689	703·7	−0·62
1·28–	530	567·6	−1·79
2·56–	231	263·7	−2·17
5·12–	150	163·7	−1·13
10·24–	96	113·8	−1·74
>20·48	112	126·4	−1·36
Summary t-values		Rank weighted	−5·95
		Dose weighted	−3·04

*Obvious factors = sex, age at hire, years worked, and year of hire.
†Expected calculated from survivors.

Table 7 *Comparing all deaths with survivors after control for job related mortality risks* in addition to obvious factors†*

Dose (rems)	Observed	Expected‡	t-value
0.00	1060	999·9	+2·42
0·01–0·07	555	570·0	−0·72
0·08–0·31	869	836·1	+1·32
0·32–	647	652·7	−0·25
0·64–	689	689·9	−0·04
1·28–	530	553·2	−1·14
2·56–	231	253·6	−1·55
10·24–	96	107·2	−1·15
>20.48	112	119·9	−0·79
Summary t-values		Rank weighted	−3·68
		Dose weighted	−1·94

*See text.
†See table 6.
‡Expected calculated from survivors.

problem. To this end two of the original 80 cohorts are shown in tables four and five as though they were the result of a designed experiment—that is, both the deaths and the distribution of cumulative dose at a given time are shown, thus making it possible to see that the death rate is reduced by high dose. The corresponding sophisticated analysis, with only statistical control for the four obvious factors mentioned above, is contained in table 6. Again there is a negative association between dose and mortality whose high significance can be seen in two summary t-valves.

The reason for having two summary statistics is as follows: in any analysis of dose response the dose weighted statistic is an obvious choice. When, however, the Hanford radiation doses were grouped on an approximately logarithmic scale the dose distribution was regular (table 6). Therefore, on a linear scale of dose the distribution would be very skew, and thus allow any dose weighted statistic to be unduly affected by a small number of workers with very high doses. Some critics have implied that

this is the *sole* reason for the controversial MSK results.[6] Therefore, a rank weighted statistic which is much less affected by extreme values is shown alongside the dose weighted statistic. A further reason for having both statistics is because comparisons between them should show whether the dose response is likely to be linear—that is, the dose weighted statistic has the higher value—or curvilinear—that is, the rank weighted statistic has the higher value.

Effect of adding differential mortality to the usual controlling factors

Table 7 shows the effect of adding five levels of differential mortality to the obvious controlling factors and table 8 shows a similar table with (B) cancers as the test group. Compared with table 6 the two summary statistics have low values. There still remains, however, a significant negative association with dose. For (A) cancers there is a positive association with dose (table 9) but this achieves statistical

Table 8   *Comparing (B) cancers with survivors after control for job risks* and obvious factors**

Dose (rems)	Observed	Expected†	t-value
0.00	96	83·7	+1·71
0·01–0·07	39	45·0	−1·00
0·08–0·31	62	66·3	−0·60
0·32–	57	49·3	+1·23
0·64–	53	54·1	−0·17
1·28–	45	42·2	+0·49
2·56–	21	19·1	+0·47
5·12–	7	12·7	−1·70
10·24–	6	8·3	−0·83
>20·48	4	9·4	−1·93
Summary		Rank weighted	−2·33
t-values		Dose weighted	−2·69

*See tables 6 and 7.
†Expected calculated from survivors.

Table 9   *Comparing cancers of radiosensitive tissues with survivors after control for job risks* and obvious factors* with no allowance for latency or age effect*

Dose (rems)	Observed	Expected†	t-value
0.00	112	119·0	−0·79
0·01–0·07	70	72·0	−0·27
0·08–0·31	102	104·4	−0·27
0·32–	89	78·9	+1·26
0·64–	94	88·6	+0·64
1·28–	70	80·4	−1·33
2·56–	39	38·0	+0·18
5·12–	28	25·0	+0·65
10·24–	17	17·6	−0·14
>20·48	22	19·2	+0·71
Summary		Rank weighted	+0·95
t-values		Dose weighted	+0·77

*See tables 6 and 7.
†Expected calculated from survivors.

Table 10   *Comparing cancers of radiosensitive tissues with survivors after control for job risks* and obvious factors* with allowance for latency only† and no age effect*

Dose (rems)	Observed	Expected†	t-value
0.00	105	113·4	−0·98
0·01–0·07	66	71·1	−0·68
0·08–0·31	99	105·9	−0·77
0·32–	96	78·8	+2·16
0·64–	77	79·5	−0·32
1·28–	52	56·8	−0·71
2·56–	33	27·8	+1·07
5·12–	20	17·6	+0·61
10·24–	17	13·5	·1·02
>20.48	7	7·7	−0·26
Summary		Rank weighted	+1·76
t-values		Dose weighted	+0·76

*See tables 6 and 7.
†Allowance for latency by discarding last 10 years of dose.
‡Expected calculated from survivors.

significance only after making some allowance for the effects of cancer latency and exposure age (tables 10 and 11).

Table 11   *Comparing cancers of radiosensitive tissues with survivors after control for job risks* and obvious factors* with no allowance for latency* of age effect†*

Dose (rems)	Observed	Expected†	t-value
0.00	114	125·4	−1·31
0·01–0·07	95	100·6	−0·67
0·08–0·31	126	110·9	+1·70
0·32–	43	56·2	−1·93
0·64–	54	53·5	+0·08
1·28–	47	44·4	−0·44
2·56–	32	34·2	−0·41
5·12–	26	20·5	+1·31
10·24–	19	12·1	−2·09
>20·48	16	14·3	+0·52
Summary		Rank weighted	+2·44
t-values		Dose weighted	+1·88

*See tables 6 and 7.
†Allowance for age effect by increasing dose by 10% for each year after age 40.
‡Expected calculated from survivors.
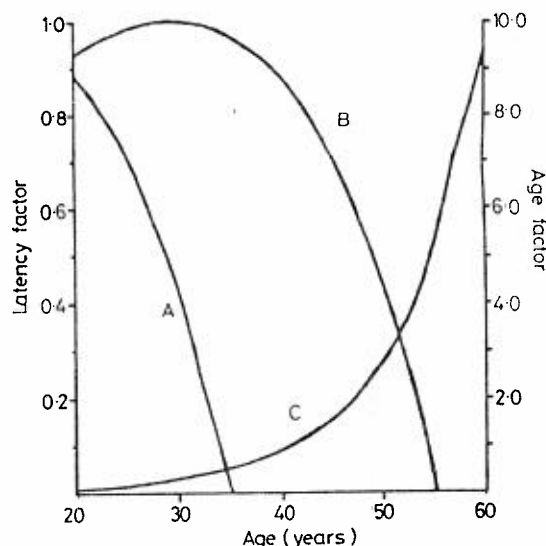
A= Latency curve for man dying age 35
B= Latency curve for man dying age 55
C= Age curve for both men

Fig. 1   *Effect of exposure age and latency on cancer risks of low level radiation (see MSK III).*

In the original analysis of Hanford data by the method of Cox[4] the effects of cancer latency and exposure age were estimated by maximum likelihood and the results were given as formulas which are graphed in fig 1. In the present analysis there is a fixed allowance of 10 years for latency and a changing allowance for exposure age by a weight which
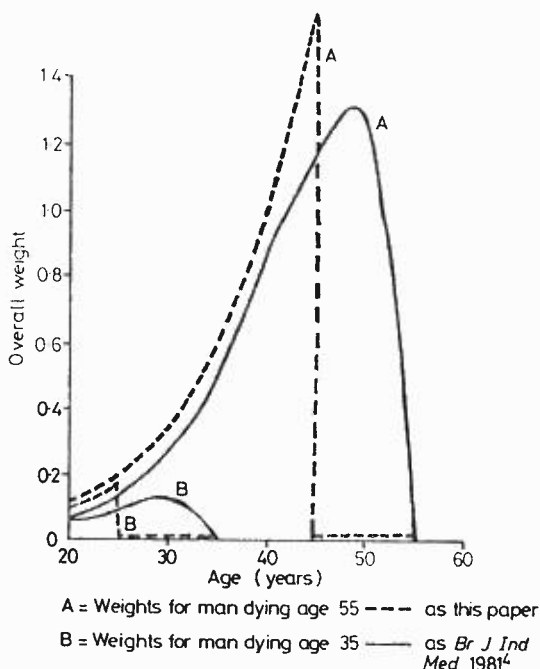
Fig. 2 *Dose weights of two workers: comparisons between current estimates and MSK III.*

increases by 10% a year. The continuous lines in fig 2 show the dose weights derived from the two formulas for two Hanford workers, and the broken lines show the dose weights derived from the present analysis. Finally, one of the conclusions of the earlier analysis was non-linearity of dose response (with the curve obeying the square root law) which is also the impression left by the two summary statistics in tables 9 and 10.

Discussion

The present analysis was the direct outcome of work which had shown that really dangerous jobs at Hanford were the prerogative of two groups of workers who had a reduced risk of dying from natural causes. Thus the principals had professional or technical qualifications that placed them in a high income bracket, and their assistants were skilled craftsmen who earned more than most manual workers. This selection bias, coupled with the fact that for all manual workers there was an *inverse* relation between differential mortality and radiation doses, made it essential to control for job related mortality risks in any study of cancer effects of the radiation.

The basic requirements for exerting this type of control were, firstly, an exact method of estimating

job related mortality risks and, secondly, a grouping of over 8000 job titles into fewer than 20 groups without destroying original associations with income and danger levels. The method of job compression was described in the earlier paper and the method of risk estimation in the present one.

There are two final conclusions. The first is that screening of death benefit claims has been reasonably successful in identifying fatal cancers but for some unexplained reason the unrecognised cases include more (B) than (A) cancers and have more low than high dose cases. The second conclusion is that for cancers of radiosensitive tissue there is a definite dose response that is curvilinear with long latency and increasing effects with increasing exposure age.

Appendix

EXACT ESTIMATES OF JOB RELATED MORTALITY RISKS

Let cohorts be indexed by g, let age be indexed by a, so that P_{ag} = probability of dying at age a in cohort g. Let workers be indexed by i, let $d_i = 1$ if worker i is dead, 0 otherwise. Let jobs be indexed by k and j. Let N_{ika} = total number of years (not necessarily consecutive) for which worker i has held job k by time he has reached age a. Let r_k (= health index of job k) be so defined that if S_{ia} (= $\Sigma N_{ika} r_k$) is the cumulative health index score of worker i by age a, then the ~~correlated~~ probability of dying (taking into account special risks of jobs and also any special "healthy worker effects" due to selective recruitment) is given by $P_{ag} \exp(S_{ia})/[1 + P_{ag} \exp(S_{ia}) - P_{ag}]$, or in other words S_{ia} is the change in the logit of the probability of dying. Then it can be shown by Cox's method of regression models in life tables that if the r_k are all compared with 1 the maximum likelihood estimates of the r_k satisfy the equations:

$$\sum_k V_{kj} r_k = Y_j$$

$$where \; V_{kj} = \sum_i \left[\sum_{a=1}^{A_i} N_{ika} N_{ija} P_{aG_i} (1 - P_{aG_i}) \right]$$

$$and \; Y_j = \sum_i \left[N_{ija} d_i - \sum_{a=1}^{A_i} N_{ija} P_{aG_i} \right]$$

and where A_i = final age of worker i and G_i = cohort of worker i.

Because of the complexity of the calculation to obtain the matrix V, and the necessity to invert this, exact estimates of mortality risks can be obtained only if the maximum number of occupational groups is in the region of 20.

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