Late Effects of Radiation

Neglected Aspects of A-Bomb Data

by

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Abstract

Following retrieval of records relating to acute effects of the Hiroshima and Nagasaki bombs, the mortality experiences of five year survivors were analysed under conditions which allowed separate recognition of persons who had sustained multiple injuries. This analysis showed that sensitivity to all effects of radiation (early and late) is exceptionally high towards the beginning and end of the life span, and that late effects of radiation include deaths from cardiovascular diseases as well as neoplasms.

Introduction

In April 1975 the Radiation Effects Research Foundation (RERF) replaced the Atomic bomb Casualty Commission (ABCC) as the body responsible for a study population assembled five years after the bombing of Hiroshima and Nagasaki (life span study or LSS cohort). As a result of this change RERF also took charge of "*a broad program of study ..... [which] represents a systematic search for mortality differentials associated into radiation ..... provides a testing ground for definite hypotheses as to delayed mortality effects ..... [and] will be as sensitive as possible to effects that are not justly conceived*"[1].

Having ascertained that close to 195,000 A bomb survivors were still living in Hiroshima and Nagasaki on October 1st, 1950, ABCC officials – who had had time to made some rough calculations of dose – decided to include in a study population '*all possible cases with appreciable amounts of radiation, and adopt a stratified plan for the rest*'[1]. They took, as cases, all survivors within 2500 meters of the two hypocentres, and had as controls, two groups from greater distances with '*the same size and the same age and sex composition as the groups under 2000 meters*'. Likewise, when it came to constructing a 'cohort of *in utero* children', they, first, ascertained from various sources that between the time of the bomb and May 31st 1946, there had been 5893 live births in Hiroshima and 4477 in Nagasaki, and then proceeded along the following lines "*All subjects in the groups within 1550 m were included in the study sample and comparison subjects were selected from each of the distance groups 1500-1599 m, 2000-2999 m, and 3000-3999 m having the same source, city and sex, and the closest match possible for month of birth*"[2].

These early decisions reveal a poor understanding of the basic requirements of epidemiological surveys: with no scope for human experimentation it is only in relation to *unmatched* factors that such surveys can advance knowledge. Therefore, deliberate matching of two sets of ABCC cases and controls for age at the time of the bomb has made it difficult for RERF to identify the separate contributions made to radiation effects by dose and ATB age. This basic weakness of A-bomb data is not widely recognised but it lies at the root of several unsolved problems.

Unsolved Problems

Though an early finding of the Oxford Survey of Childhood Cancers (OSCC) was compatible with a single *in utero* exposure to a small dose of radiation being sufficient to increase the risk of an early cancer death[3], there were no counterpart findings for A-bomb survivors[4]. It is customary to ascribe this discrepancy either to faulty interpretation of OSCC data[5], or the small size of the *in utero* cohort[6]. But, as a result of Kneale discovering that there is mounting sensitivity to infections during the latent phase of leukaemia[7,8], Stewart suggested, first, that the total absence of any early deaths from leukaemia in the cohort of *in utero* children might be the result of selective loss of infection sensitive children during the immediate aftermath of the bombing[9] and, later, that the normal noncancer death rate of the LSS cohort might be an artifact caused by opposite effects of selection and marrow damage[10,11].

For RERF – whose linear model of relative risk was constantly leaving an impression of no late effects of radiation except cancer[12] – there was no need for these conjectures. Under pressure from Stewart, they had been forced to admit that "*with mortality in the immediate areas of the hypocenter essentially 100% ..... and falling*

rapidly with increasing distance from the hypocenter, selection was an indubitable fact, and not an issue"[13]. But they still insisted *"The A bomb population is a highly selected one, of course, but that its selection has made it unrepresentative with respect to the carcinogenic effect in man, has not been shown."*

This position *vis a vis* A-bomb data persisted in spite of an independent analysis of LSS data showing that, for noncancer deaths there was a biphasic dose response curve with its lowest point close the dose required for nonstochastic effects of radiation[14]. This new development was the result of Kneale realising that although, with a linear model of relative risk, opposite effects of selection and marrow damage might leave an impression of neither effect, they were unlikely to be *exactly* equal and opposite. He therefore used a different model, and thus, found evidence of two (contrasting) effects of the radiation.

There followed further tests of LSS data by Stewart and Kneale, which showed that, in spite of the ATB age matching, the proportion of high dose survivors (over 1 Gy) was well below average for persons who were under 10 or over 50 years of age when exposed[15]. This observation was clearly the result of deaths before 1950 being a special risk of children and old persons, but still lacking was any evidence that this selection had made the LSS cohort *"unrepresentative with respect to the carcinogenic effect in man"*[13]. To settle this point it was necessary to know more about the persons who had actually sustained acute injuries. There might be difficulty in discovering who had survived acute marrow damage, but, in 1965, Jablon *et al* had identified survivors with burns, oropharyngeal lesions, purpura and epilation (and decided that these data only had 'descriptive value')[16] and, in 1989, Neriishi *et al* had shown that for persons

with epilation, the dose response curve for leukaemia deaths was exceptionally steep[17]. Therefore, RERF were approached and kindly agreed to release the following data.

RERF Data

The tables released by RERF described the LSS cohort as it was in October 1950 and gave the person-years at risk of any later deaths. In addition to the usual stratification by sex, city, ATB age, DS86 dose and interval between death and starting date, there was also stratification by four types of acute injury (burns, oropharyngeal lesions, purpura and epilation) under three headings: claimed, denied or no record (Table 1), and in each stratum of the data, deaths were classified under six headings: leukaemia, other malignant neoplasms, benign tumours, trauma, cardiovascular diseases (Table 2). In this table each cause of death and several levels of DS86 doses are classified by the overall frequency of acute injuries (after removal of 1949 survivors who had no record of any injuries). This arrangement of the data discloses an exceptionally strong association between injuries and leukaemia and shows one effect of the missing records of marrow damage: doses sufficient to have nonstochastic effects were not confined to survivors with obvious injuries.

Statistical Analyses

1) Analysis of Variance

The first of several analyses drew a distinction between the four types of injury and was essentially an analysis of variance of 'age specific mean dose' after subdivision of the whole LSS cohort into the 12 subgroups of Table I. The results of these tests are shown in the first half of Table 3 under the following headings: numbers of persons with each type of injury (N); the mean dose in mGy; two sets of standard

errors (S_1 and S_2), two t values (linear and quadratic), and a single chi square. S_1 corresponds to the mean square dose for all survivors in the same exposure age group, so it has N minus 13 degrees of freedom. S_2 corresponds to the between age group sum of squares (after removal of the ones for the grand mean and the linear and quadratic components of the trend of age specific doses), so it has 10 degrees of freedom The two t values assess the significance of linear and quadratic dose trends, and the single chi-square assesses the joint significance of the two trends. Therefore, we have $(S_1:S_2)^2$ providing an F test of general homogeneity of the dose for each type of injury (Fisher analysis of variance), while t values and chi-squares provide tests of subgroup homogeneity for linear and quadratic components of dose trend.

These tests revealed complex patterns of heterogeneity, with no dominant effect of any one type of injury. Therefore, in all subsequent analyses there was pooling of the various injuries to produce the four levels of overall injury frequency as in Table 2. The results of repeating the analysis of variance after making this change are shown in the second half of Table 3. Once again there were complex patterns of subgroup heterogeneity, with no consistent pattern for linear or quadratic components of the dose trend.

2) Poisson Regression

These analyses were similar to the ones in BEIR V[6]. They were essentially Poisson regressions of mortality rates on dose, though the regression was of the natural logarithm of the relative risk, not the excess relative risk (as in BEIR V). This was necessary in order to cope with the extra stratification by three levels of four types of injury. The risk model parameters were log relative risks at 1 Gy for the seven ATB

age groups in Table 5. There was an eighth parameter (not shown in the table) to allow for possible variation of latency with exposure age. This was achieved by only including a stratum if the mean interval to death (after person-year weighting) was greater than a certain multiple of the person-year weighted mean exposure age, and for each parameter of the model there was a maximum likelihood estimate.

With several standard packages to choose from, the maximisation method actually used was the simplex method of Nelder and Mead[18] since this is robust and does not require calculation of differential coefficients. Unfortunately, the Nelder and Mead method is not suitable for estimating standard errors of parameters. Consequently all the statistical tests are in the form of likelihood ratios. The chi-squares for testing the null hypothesis of no radiation effects are minus twice the natural logarithm of the likelihood ratio; and the tests of whether (in subsets defined by the frequency of acute injuries) the model parameters were homogenous, were made by comparing sums of chi-squares for each subgroup (calculated separately) with the chi-square for all subgroups and assuming homogeneity at this level (Table 5).

Results of the Poisson Regression Tests

In Table 4 – where there are eight causes of death, seven ATB ages, and six subsets of LSS data – and in Fig. 2 – whose numerical basis can be found in Table 4 – there is evidence that late effects of the radiation included deaths from cardiovascular diseases as well as cancers and benign tumours; also evidence that these effects were different for survivors with and without multiple injuries; and different again for survivors who were under 10 or over 60 years of age in 1945.

Further evidence of noncancer effects of the radiation as well as ATB age effects, can be found in Table 5. Here there are two sets of chi squares: one to show that, for several causes of death, there was firm rejection of the hypothesis of no radiation effects (see the six subgroups of LSS deaths, as in Table 4); and one to show that there were significant differences between survivors with and without multiple injuries (see *equivalent* subgroups of LSS deaths).

Finally, in Table 6, where linear and quadratic regression coefficients at 1 Gy are shown for three levels of ATB age and four types of neoplasms (and in Fig. 2, where there are dose response curves for all neoplasms) one can see that late effects of the A-bomb radiation were different for survivors with and without multiple injuries, and that all the significant differences came from exposures before 5 or after 59 years of age.

Discussion

There would seem to be two reasons why RERF failed to recognise that towards the beginning and end of the natural life span persons are exceptionally sensitive to late as well as early effects of radiation: the deliberate matching of two sets of ABCC cases and controls for ATB age; and the exclusion of all data relating to acute injuries from tests of radiation effects. Coming on top of the first mistake the second one was particularly unfortunate since all that was needed to reveal the true situation was a variable which reflected the intensity of the early selection. This was a key factor since it left the high dose subgroups of the LSS cohort short of children and old persons, but also left the cohort of *in utero* children in no position to observe late effects of near conception exposures[15].

So far as the LSS cohort was concerned, all that was needed was retrieval of the injury data which had been set aside in 1965[16]. By incorporating these data in a Poisson regression analysis it was possible to see that, besides to being more likely to die from acute effects of the bombing than young adults, children and old persons were more likely to experience late effects of the radiation; and to see that, besides causing leukaemia and malignant tumours, late effects of the radiation included deaths from cardiovascular diseases and benign tumours.

The findings for deaths ascribed to cardiovascular diseases agree with recent work by Shimizu *et* al[19], and make it probable that nonstochastic effects of the radiation were responsible for some of the LSS deaths. Given the many reasons for fatal thromboses and cardiac insufficiency in elderly persons, and the fact that deaths from the one distinctive effect of marrow damage (aplastic anaemia) continued long

after 1950[13], we could witnessing both the effects of irreversible damage to the reticulo-endothelial system and the effects of somatic mutations.

With so many deaths of children and old persons before 1950, there was a distinct possibility that, in the Poisson regression analysis, late effects of the radiation would be *less* obvious for survivors with than without multiple injuries. The opposite finding testifies to the strength of the association between exposure age and late effects of radiation, and makes it tempting to suggest that in all populations there are subsets of persons with immune system weaknesses that make them *hypersensitive* to all carcinogens. Known reasons for this hypersensitivity include ataxia telangiectasia, Fanconi's anaemia, and Down's syndrome[20]. These congenital anomalies carry a high risk of early death, but there might be other constitutional or life-style factors which have similar effects at much later ages (and might be identified through A-bomb data).

Meanwhile, although one weakness of A-bomb data has been removed there remains a second weakness which affects all surveys where the upper limit of dose exceeds the threshold for nonstochastic effects. At this high dose level radiation not only has cancer promoter effects (*via* marrow damage) but also increases the demand for myelocytes[21]. Whether these reactions are responsible for the special bond between myeloid leukaemia and radiation in A-bomb data and the ankylosing spondylitis survey[22] is far from certain. But this special relationship was conspicuous by its absence both in OSCC data[3] or in three sets of occupational data[23-25]. So there remains both a possibility that what is usually regarded as a typical, stochastic effect of radiation actually requires a combination of cell killing and mutational effects[21] and a possibility that this combination was the reason why, in Table 2, so many of the injured survivors eventually developed leukaemia.

Legend to Figures

Fig. 1 Natural logarithm of relative risk at 1 Gy for six causes of death at three ATB age levels

Fig. 2 Dose response curves for all fatal neoplasms at three ATB age levels

Fig 1

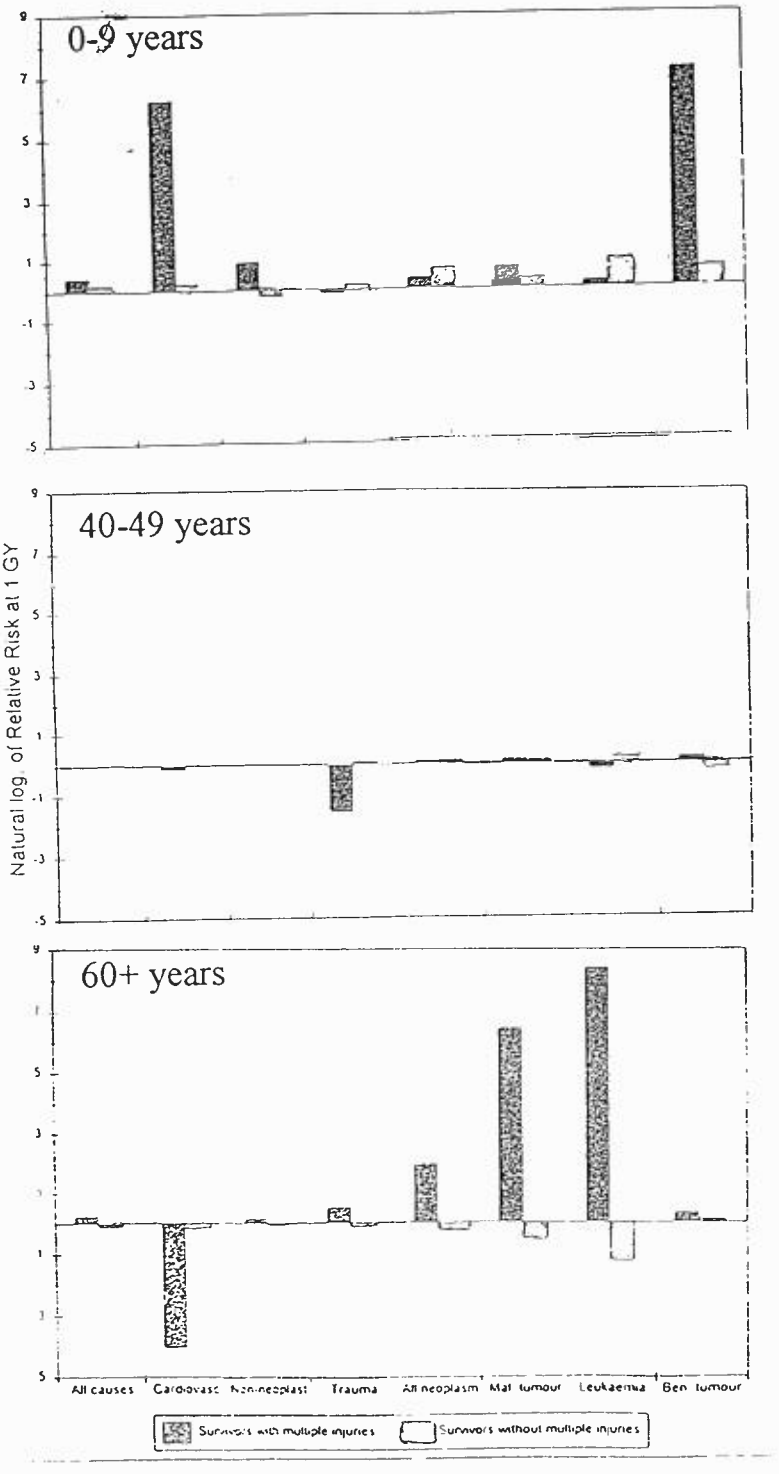
0-9 years
40-49 years
60+ years
Natural log. of Relative Risk at 1 GY
All causes
Cardiovasc
Non-neoplast
Trauma
All neoplasm
Mal tumour
Leukaemia
Ben tumour
Survivors with multiple injuries
Survivors without multiple injuries

fig 2

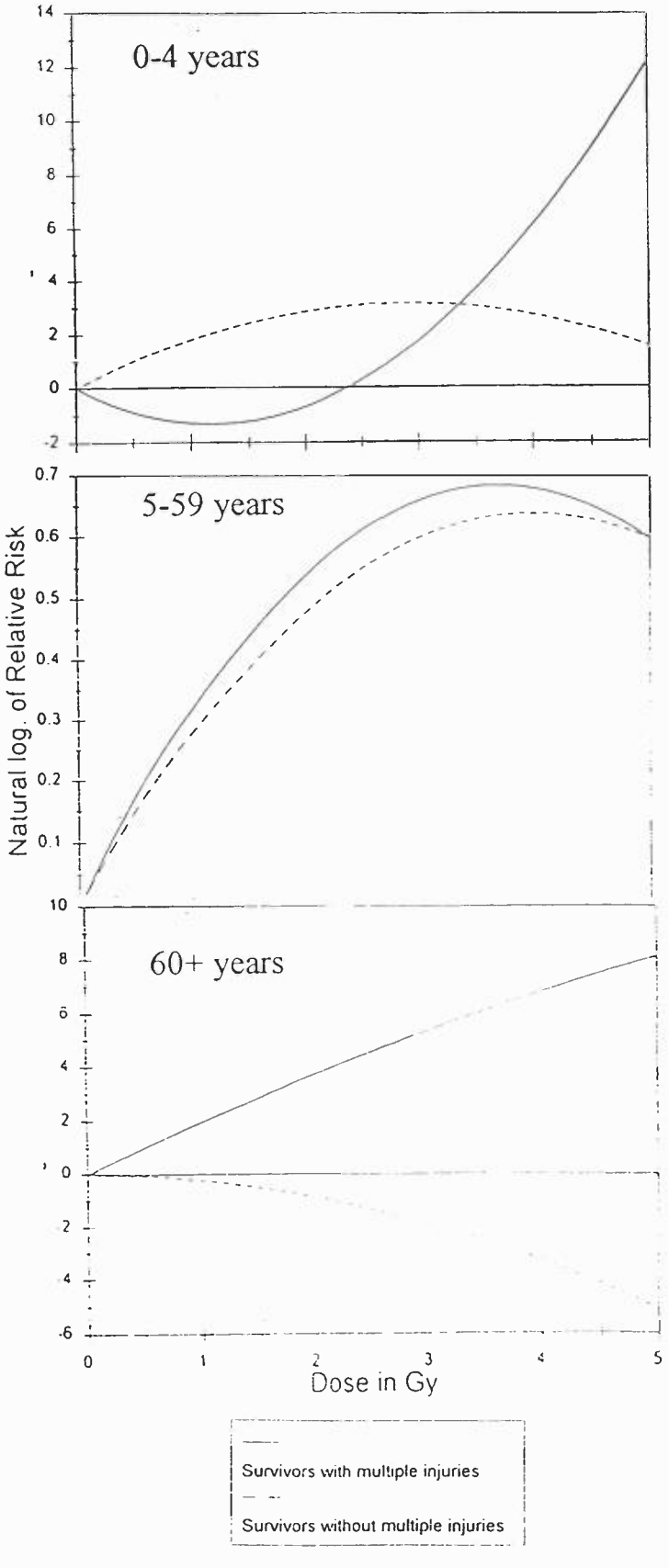
0-4 years
5-59 years
60+ years
Natural log. of Relative Risk
Dose in Gy
Survivors with multiple injuries
Survivors without multiple injuries

Table 1 LSS Data for Four Types of Acute Injury

Acute Injury	Claimed	Denied	No Record[(1)]
Burns	5,551	67,745	2,695
Oropharyngeal Lesions	3,613	69,640	2,738
Purpura	2,432	70,930	2,629
Epilation	1,308	71,982	2,701

(1) Including 1949 survivors who neither claimed nor denied any one of the four injuries.

Table 2 Overall Frequency of Acute Injuries by Stated Cause of Death and DS86 Dose Estimates

Specifications		Number of Deaths Acute Injuries[1]					Any Injury %
		Nil[c]	Nil[i/c]	One	Multiple	Total	
Stated Cause of Death	Leukaemia	121	8	31	41	210	34.3
	Other Malignant Neoplasms	4,487	138	570	296	5,491	15.8
	Benign Tumours	224	6	31	12	273	15.8
	Trauma	1,181	35	142	52	1,410	13.8
	Cardiovascular Diseases	9,073	257	984	362	10,676	12.6
	Other or Unspecified	7,721	235	814	309	9,079	12.4
	All Causes	22,807	679	2,572	1,072	27,130	13.4
DS86 Dose in mGy	0-4	31,138	682	1,253	147	33,220	4.2
	5-94	24,422	622	2,231	408	27,683	9.5
	95-494	6,744	295	2,367	691	10,097	30.4
	495-994	609	56	552	725	1,942	65.8
	995-1994	95	22	158	360	635	81.6
	1995-2994	33	5	38	136	212	82.1
	2995+	31	4	84	134	253	86.2
Total		63,072	1,686	6,683	2,601	74,042	12.5

(1) Excluding 1949 survivors with 'no record' for each type of injury

(2) Nil[c] four denials

Nil[i/c] no injuries claimed but one or more 'no records'

Table 3 **Analysis of Variance: Tests of Various Age Related Effects of Radiation**

Specifications			No. Persons (N)	Mean Dose mGy	Components of the S.E. of Dose		t value		Chi Square[5]
					S1[3]	S2[4]	Linear	Quadratic	2 df
Type of Acute Injury[1]	Burns	claimed	5,551	561.3	954.1	1424.3	-1.79	-1.77	5.56
		denied	67,745	134.0	413.6	1046.3	+0.46	*-2.38**	6.81
		no record	2,695	36.2	167.9	143.4	-0.47	+0.81	0.70
	Oropharyngeal	claimed	2,433	1051.2	1220.8	1080.1	*-2.41**	*-2.28**	*10.32**
		denied	70,930	131.1	398.3	704.4	+0.74	-1.13	2.36
		no record	2,628	167.6	563.4	618.3	*-8.43***	+1.35	*77.31***
	Purpura	claimed	3,613	1050.3	1176.3	1759.4	*-2.53**	-1.23	*7.34**
		denied	69,640	114.7	354.1	387.9	*+1.92**	+1.47	4.76
		no record	2,738	187.5	586.6	495.4	*-10.33***	+1.39	*118.53***
	Epilation	claimed	1,308	1993.1	1437.5	1626.9	*-2.88**	*-2.56**	*11.26**
		denied	71,981	128.3	370.1	738.0	*+2.05**	*-2.28**	*12.33**
		no record	2,702	166.7	488.4	539.7	*-7.91***	+0.21	*73.48***
Frequency of any Injury[2]	No. of Injuries	Nil[c]	63,072	84.7	252.5	495.3	*+2.14**	*+2.27**	*7.78**
		Nil[1/c]	1,686	205.1	251.5	487.2	*-2.23**	*+2.11**	*10.39***
		One	6,683	449.6	783.5	550.7	*-2.17*	*+5.37***	*39.06***
		Multiple	2,601	1355.4	1320.2	1411.5	*-4.07***	*-0.70*	*16.60***
	Total		74,042	165.0	489.8	1071.0	*+0.02*	*-4.22***	*18.91***

(1) Including 1949 survivors who neither claimed nor denied anyone of the four injuries (see Table 1)
(2) Excluding 1949 survivors who neither claimed nor denied anyone of the four injuries (see Table 2)
(3) S1 is the standard error of the dose for all persons in the same exposure age group (d.f. N-13)
(4) S2 is the standard error of dose between exposure age groups (d.f. 10)
(5) Total for the combined effect of the linear and quadratic components of dose trends

* = $p>0.05$
** = $p>0.01$

Table 4 **Cause of Death by Age at Time of the Bomb**

Natural logarithms of the relative risk at 1 Gy (or excess relative risk)

Cause of Death	ATB Age[1] in Years	Natural logarithms of relative risk at 1 Gy Subgroups of LSS Deaths[2]					
		I	II	III	IV	V*	VI
All Causes	0-	0.33	0.36	0.31	*0.32*	*0.45*	0.26
	10-	0.12	0.20	0.08	0.17	0.01	0.14
	20-	0.15	0.24	0.11	0.12	0.21	0.03
	30-	0.16	0.19	0.13	0.12	0.20	-0.01
	40-	0.01	0.05	-0.00	*0.03*	*-0.01*	0.01
	50-	0.04	0.04	0.01	0.05	-0.05	0.05
	60+	-0.07	-0.13	0.05	*-0.11*	*0.26*	-0.00
	No. of Deaths	27,130	22,807	4,323	26,058	1,072	3,251
Cardiovascular Diseases	0-	+0.38	-0.32	+1.03	*+0.25*	*+6.26*	0.71
	10-	-0.04	-0.10	-0.02	-0.39	+0.50	-0.79
	20-	+0.15	-0.36	+0.28	-0.07	+.045	0.14
	30-	+0.22	+0.15	+0.27	+0.17	+0.33	0.19
	40-	-0.03	-0.02	-0.04	*+0.01*	*-0.15*	0.03
	50-	+0.07	+0.04	+0.14	+0.05	+0.49	0.07
	60+	-0.16	-0.23	-0.04	*-0.14*	*-4.06*	0.04
	No. of Deaths	10,676	9,073	1,603	10,314	362	1,241
Other Non-Neoplastic Diseases	0-	-0.06	-0.04	-0.11	*-0.21*	*+0.92*	-0.76
	10-	0.10	0.03	0.12	0.16	-0.06	0.23
	20-	0.05	0.24	-0.05	-0.05	+0.28	-0.67
	30-	0.11	0.17	0.06	0.13	+0.04	0.04
	40-	0.01	-0.09	0.05	*0.00*	*+0.02*	0.04
	50-	0.02	0.03	0.01	0.05	-0.11	0.10
	60+	-0.05	-0.09	-0.00	*-0.06*	*+0.17*	0.04
	No. of Deaths	9,079	7,721	1,358	8,770	309	1,049
Trauma	0-	0.08	-0.09	+0.20	*+0.15*	*-0.15*	+0.41
	10-	0.07	0.23	-0.07	+0.07	+0.07	-0.10
	20-	-0.25	-0.31	-0.17	-0.32	+1.67	-0.32
	30-	-0.17	0.25	-0.60	-0.16	-0.18	-1.36
	40-	-0.10	0.05	-0.24	*+0.10*	*-1.55*	+0.17
	50-	-0.11	-0.04	-0.19	-0.25	+0.80	-0.55
	60+	-0.16	-0.07	-0.31	*-0.16*	*+0.53*	+0.46
	No. of Deaths	1,410	1,181	229	1,358	52	177

continued on next page

Continuation of Table 4

All Neoplasms	0-	0.65	0.75	0.31	*0.69*	*0.38*	0.24
	10-	0.23	0.36	0.12	0.34	-0.09	0.29
	20-	0.23	0.50	0.14	0.31	0.06	0.21
	30-	0.16	0.24	0.11	0.10	0.23	-0.18
	40-	0.10	0.25	0.01	*0.11*	*0.11*	-0.14
	50-	-0.02	0.07	-0.11	0.05	-0.44	0.10
	60+	-0.09	-0.32	0.19	*-0.25*	*1.96*	-0.29
	No. of Deaths	5,965	4,832	1,133	5,616	349	784
Solid Tumours	0-	0.41	0.48	0.29	*0.37*	*+0.74*	0.13
	10-	0.27	0.37	0.19	0.36	-0.06	0.36
	20-	0.22	0.49	0.11	0.30	+0.01	0.19
	30-	0.16	0.26	0.10	0.10	+0.22	-0.18
	40-	0.11	0.25	0.03	*0.11*	*+0.14*	-0.15
	50-	-0.03	0.05	-0.14	0.09	-0.47	0.10
	60+	-0.19	-0.48	0.72	*-0.56*	*+6.47*	-1.00
	No. of Deaths	5,491	4,487	1,004	5,195	296	708
Leukaemia	0-	0.93	1.04	0.32	*0.97*	*+0.23*	0.46
	10-	0.07	0.46	0.05	0.17	-0.06	-0.04
	20-	0.24	-0.31	0.28	0.11	+0.23	0.57
	30-	0.29	0.05	0.38	0.07	+0.37	0.47
	40-	-0.05	0.07	-0.05	*0.23*	*-0.20*	0.17
	50-	0.59	0.59	0.40	0.61	-15.29	1.03
	60+	-0.58	-0.07	-0.35	*-1.29*	*+8.41*	0.14
	No. of Deaths	201	121	80	160	41	39
Benign Tumours	0-	0.63	0.64	2.31	*0.64*	*7.22*	27.39
	10-	-0.60	0.01	-0.94	-0.23	-1.43	-0.65
	20-	0.46	1.01	0.06	0.62	-0.16	0.10
	30-	-0.70	-0.10	-1.98	-0.29	-10.13	-1.19
	40-	-0.06	0.17	-0.43	*-0.13*	*0.18*	-0.59
	50-	-0.24	-0.42	-0.14	-0.26	-0.20	-0.05
	60+	0.12	0.83	0.02	*0.12*	*0.34*	-19.75
	No. of Deaths	273	224	49	261	12	37

(1) ATB age = age at the time of the bomb

(2) I All deaths
II Excluding injuries and incomplete records
III Residue
IV Excluding multiple injuries
V Multiple injuries
VI Single injury

* for figures in italics see Fig. 1

Table 5 **Cause of Death by the Age when Exposed to Radiation**

Tests of the null hypothesis of no radiation effects and no subgroup heterogeneity

Causes of Death (No. of Deaths)	Chi Squares[1] Subgroups of LSS Deaths[3]						Chi Squares[2] *Equivalent* Subgroups of LSS Deaths[3]			
	I	II	III	IV	V	VI	I	II+III	IV+V	II+V+VI
All Deaths (27.130)	41.07*	29.55*	15.66*	30.25*	15.24*	5.89	41.07	45.21 *4.14*	45.49 *4.92*	50.68 *9.61*
Cardiovascular (10,676)	17.14*	5.97	22.67*	8.89	34.52*	0.17	17.14	28.64 *11.50*	33.41 *16.27**	40.66 *23.52**
Other Diseases (9,079)	3.32	4.24	2.56	5.46	5.89	10.56	3.32	6.80 *3.48*	11.32 *8.00*	20.66 *17.32*
Trauma (1,410)	1.94	2.41	5.10	2.78	7.81	9.26	1.94	7.51 *5.77*	10.59 *8.65*	19.48 *17.54*
All Neoplasms (5,965)	58.60*	58.61*	7.65	40.74*	17.64*	9.73	58.60	64.26 *7.66*	58.38 *0.22*	85.98 *27.38**
Solid Tumours (5,491)	25.79*	31.92*	8.07	27.73*	20.76*	10.51	25.79	39.99 *14.20**	48.49 *22.70**	63.22 *37.43**
Leukaemia (201)	32.82*	34.99*	4.20	33.97*	3.71	2.56	32.82	39.19 *6.63*	37.68 *4.86*	41.26 *8.44*
Benign Tumours (273)	5.06	5.24	4.95	4.13	4.21	4.65	5.06	10.19 *5.13*	8.34 *3.28*	14.10 *9.04*

(1) For testing the null hypothesis of no radiation effects (8 d.f.)

(2) For testing the null hypothesis of no significant differences between the subgroups of LSS deaths (16 d.f. for II+V+VI, otherwise 8 d.f.)

(3) as in Table 4

* Significant chi squares

Table 6 **Neoplastic Deaths of Survivors with and without Multiple Acute Injuries**

Linear and Quadratic Regression Coefficients at 1 Gy

Specifications	ATB Age	Regression Coefficient at 1 Gy	All Neoplasms*	Leukaemia	Malignant Tumours	Benign Tumours
Survivors With Multiple Injuries	0-4	Linear	*-2.21*	-0.23	2.68	-17.39
		Quadratic	*0.93*	2.23	-5.13	0.24
	5-59	Linear	*0.37*	1.28	0.23	-0.64
		Quadratic	*-0.05*	-0.23	-0.03	0.03
	60+	Linear	*2.03*	0.89	-2.58	80.48
		Quadratic	*-0.08*	0.91	5.16	45.04
	Chi-Square (7 d.f.)(1)		*15.63**	*10.04*	*11.69*	*3.54*
Other Survivors	0-4	Linear	*2.16*	3.71	0.99	2.87
		Quadratic	*-0.37*	-0.65	-0.25	-1.19
	5-59	Linear	*0.32*	0.86	0.31	0.91
		Quadratic	*-0.04*	-0.10	-0.04	-0.57
	60+	Linear	*-0.02*	-0.74	-0.27	1.46
		Quadratic	*-0.20*	-2.42	-0.22	-0.29
	Chi-Square (7 d.f.)(1)		*56.48***	*55.94***	*25.06***	*5.33*

(1) Chi square tests of the null hypothesis of no radiation effects

Figures in italics see Fig. 3

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