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FILE CODE <i>2.3 Mancuso</i>				TO Walter H. Weyzen

SUBJECT (Unclassified)  
Regarding Analysis Of Hanford  
Proportional Mortality Data,  
Adjusted For Age And Year Of Death

INFORMATION

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FOLDER 2.3 MANCUSO PROJECT (MORTALITY DATA)  
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Analysis of Hanford Proportional Mortality Data, Adjusted for Age  
and Year of Death

The analysis summarized in the attached tables was done to investigate the suggestion that some of the results reported by Mancuso, Stewart, and Kneale may be explainable as artifacts of their analysis. The approach has been to adjust for certain possible confoundings, viz., association of cumulative dose with age of death and year of death, and possible selection factors between exposed and non-exposed workers; to compute test statistics that do not assume a symmetric distribution for dose; and to analyze the death certificate data provided by ORNL in sufficient detail that some judgment can be made as to the extent of the bias introduced by a proportional mortality analysis, and as to whether the reported radiation effects could be extreme results to be expected by chance alone from a large number of investigations.

The basic statistical procedure has been a contingency table method, adjusted for age at death ( $\leq 49$ , 50-64, 65+) and year of death (1943-60, 1961-67, and 1968-73). At each level of these factors (e.g.,  $\leq 49$  and 1943-60,  $\leq 49$  and 1961-67, etc.)  $2 \times k$  ( $k=6$  and  $11$ ) contingency tables were tabulated, rows corresponding to death from a specified disease or from other causes and columns to non-exposed and to dose intervals within the exposed class. Expected cell frequencies, variances, and covariances were computed from row and column sums, and then summed over tables to provide details of the null-hypothesis distribution of the summary tables.

The main statistical results are the p-values for the exposed vs. non-exposed comparison and for the test of linear trend with dose adjusted

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for exposure; a value near one of the latter indicates a positive association of the corresponding cause of death with cumulative dose, a value near zero indicates a negative association. Extreme p-values for the exposed - non-exposed comparison, in the absence of a dose response, suggest selection of the exposed or non-exposed population for reasons related to health. An extreme p-value for linear trend unadjusted for exposure, with more moderate p-values for the main two statistics, might suggest a true dose response, especially if the adjusted trend statistic is at a "suggestive" level. The trend statistics for the cube root of dose were included as a check on the possible effects of skewness of the dose distribution.

The finer dose intervals in the 11-interval tables provide greater power against increasing trends; the 6-interval tables provide a check against numerical or distributional instability of the test statistics.

Analyses were performed for cumulative dose at death, and at 3, 5, 10, 15, and 20 years prior to death. Cancers were treated separately for each 3-digit ICD code, and in broader groups. Non-cancers were treated in broad groups, except for chronic bronchitis and emphysema, which were treated individually.

Several causes of death were present much more, or much less, in the exposed than in the non-exposed, indicating that the groups probably were selected on some basis related to health. Two cancers, pancreatic cancer and multiple myeloma, were significantly related to dose among males. One non-cancer, chronic MI, consistently decreased with increasing dose. Since the results for pancreatic cancer and multiple myeloma are based on relatively few cases, it seems unlikely that these results could be ascribed to a defect

of the proportional mortality approach; selection of the exposed population, even differentially by dose, could not be expected to create an apparent dose relationship for these diseases alone. However, a closer examination of each of the individual diagnoses would be in order, since only a few misdiagnoses could have created the effects. Pancreatic cancer, in particular, has a relatively low percentage of histologically proven cases compared with other cancer sites, and therefore may be unusually subject to misdiagnosis on death certificates. Cancers of the lung, brain, and female breast appeared to be related to dose in unadjusted contingency table analyses, but these apparent relationships did not survive adjustment for age and year of death.

[The possibility that the results for pancreatic cancer and multiple myeloma are statistical flukes, which might be expected to be obtained in an analysis of many different causes of death, cannot be ruled out. This seems less likely for multiple myeloma than for pancreatic cancer, however, since multiple myeloma is a very rare disease and the dose distribution of the cases is extreme. Excess risks of multiple myeloma and pancreatic cancer, among other cancers, have been reported among U.S. and British radiologists. On the other hand, the evidence for a dose response for these two diseases among Japanese A-bomb survivors is very weak.] It is somewhat surprising that evidence for a dose effect among Hanford workers should involve these two diseases and not leukemia or malignant lymphomas other than multiple myeloma.

Hanford males: proportional mortality analysis, adj for age + year of death

Cause + ICD	Total NE	Cum dose at death											E-NE	ln E	ln cum dose	ln E	11-dose interval ln E of cum dose at death					
		0-2	3-4	5-6	7-8	9-10	11-20	21-40	41-60	61-10	10-1+	-3					-5	-10	-15	-20		
Se. lymphatic	66	19	15	11	2	2	1	6	4	0	2	4	.914	.987	.937	.669	.786	.919	.858	.927	.999	.760
200-209	24.2	12.9	6.0	3.7	2.9	2.2	6.5	3.3	1.0	1.3	1.9											
Lymphosarcoma	19	3	3	4	2	2	0	2	2	0	1	0	.978	.313	.548	.972	.452	.361	.443	.675	.599	.761
200	7.2	3.8	1.8	1.1	0.8	0.6	1.8	0.9	0.3	0.3	0.5											
Leukemia dia	13	3	2	2	0	0	0	3	2	0	1	0	.915	.619	.753	.855	.816	.598	.246	.232	.272	.214
201	5.3	2.4	1.2	0.7	0.6	0.4	1.1	0.6	0.2	0.2	0.3											
Mult. myeloma	11	3	4	0	0	0	1	0	0	0	3	.641	.999	.999	.956	.989	.999	.999	.999	.999	.999	.760
203	3.7	2.2	1.0	0.6	0.5	0.4	1.2	0.6	0.2	0.3	0.4											
Malignant leuk	12	6	2	2	0	0	0	1	0	0	1	.100	.641	.504	.363	.449	.631	.352	.376	.471	.491	
205	3.9	2.3	1.0	0.6	0.6	0.4	1.4	0.7	0.2	0.3	0.5											
Respiratory	4	1	2	1	0	0	0	0	0	0	0	.663	.209	.257	.078	.181	.233	.255	.309	.309	.272	
210-229	1.4	0.8	0.4	0.2	0.2	0.2	0.4	0.2	0.1	0.1	0.1											
Urinary	6	5	0	0	0	0	1	0	0	0	0	.610	.470	.223	.552	.503	.456	.487	.531	.775		
230-239	2.3	1.2	0.6	0.4	0.3	0.2	0.5	0.2	0.1	0.1	0.1											
Endocrine dia	61	22	13	8	3	2	3	6	0	0	1	3	.556	.743	.747	.475	.541	.638	.472	.517	.525	.944
240-279	22.5	12.2	5.7	3.7	2.9	2.1	5.7	2.7	1.0	1.0	1.5											
Stomach	4	3	0	1	0	0	0	0	0	0	0	.093	.515	.341	.521	.511	.537	.544	.587	.574	.763	
280-289	1.7	0.9	0.4	0.3	0.2	0.1	0.3	0.1	0.0	0.0	0.0											
Heart	22	7	5	2	1	0	0	6	0	0	1	.746	.640	.704	.585	.493	.702	.732	.803	.423	.513	
320-359	8.3	4.3	2.0	1.3	1.1	0.8	2.0	1.0	0.4	0.4	0.5											
Ischemic heart	1402	507	294	124	104	64	52	128	57	17	27	29	.967	.318	.533	.414	.439	.304	.386	.295	.094	.007
410-414	532.6	284.3	135.2	86.2	63.3	45.8	124.2	54.8	20.3	20.1	31.5											
Coronary MI	1080	364	224	103	86	49	41	101	47	13	26	26	.919	.710	.944	.815	.672	.647	.732	.519	.179	.287
410-411	411.3	212.0	134.3	65.6	47.7	34.8	95.7	46.2	15.6	15.8	24.6											
Chronic MI	323	143	70	21	19	15	11	27	10	4	1	3	.003	.045	.008	.030	.016	.070	.064	.158	.305	.011
412-414	121.3	66.3	31.3	20.7	15.5	11.0	28.5	12.6	4.7	4.3	6.9											
CVD	222	80	50	25	12	16	7	16	6	3	1	6	.752	.601	.672	.370	.419	.675	.564	.469	.677	.941
430-439	85.2	46.3	22.0	15.0	10.7	7.5	18.1	7.7	2.8	2.6	4.1											
Other	260	114	58	14	14	8	5	23	11	4	3	6	<.05?									
440-449	99.2	52.6	24.5	16.2	11.7	8.6	22.9	10.8	3.6	3.9	5.9											
450-459	45.8	24.5	12.5	6.2	4.1	2.9	10.8	3.6	3.9	5.9												
Resp. dia	194	87	31	17	10	10	6	16	8	4	3	2	.017	.429	.213	.684	.677	.528	.604	.377	.530	.564
460-519	73.0	39.8	19.0	12.7	9.4	6.8	16.7	7.4	2.7	2.6	4.0											
Chronic bronch	16	5	5	1	1	1	0	2	0	1	0	0	.683	.260	.328	.251	.155	.297	.321	.431	.691	.976
491	6.0	3.3	1.6	1.1	0.8	0.6	1.3	0.6	0.2	0.2	0.3											
Empyema	79	33	8	6	4	6	3	8	7	2	0	2	.119	.615	.559	.921	.797	.780	.903	.506	.526	.461
492	28.1	16.0	7.6	4.9	3.9	2.7	7.7	3.5	1.4	1.3	2.0											
Diastolic dia	140	54	31	13	6	0	5	15	7	3	2	4	.368	.610	.567	.537	.711	.714	.646	.694	.991	.997
520-577	52.2	28.0	13.2	8.2	6.0	4.4	13.0	6.6	2.2	2.5	3.7											
Stroke	44	21	9	3	2	3	2	2	2	0	0	0	.101	.166	.097	.166	.151	.172	.196	.152	.213	.322
580-629	17.2	8.9	4.3	2.8	2.0	1.6	3.6	1.7	0.6	0.5	0.8											
Colorectal	243	98	54	25	9	14	2	21	9	3	1	7	.407	.677	.644	.476	.526	.693	.796	.108	.108	.120
600-699	95.9	47.0	23.4	15.3	12.3	8.4	17.6	9.9	2.7	3.6	5.0											
Stomach	32	14	4	5	2	1	1	3	2	0	0	0	.431	.235	.232	.377	.191	.240	.241	.320	.58	.72
6-136	13.6	6.4	2.9	2.0	1.4	1.0	2.2	1.1	0.3	0.3	0.5											
Lymphomas	52	16	12	9	2	2	1	6	4	0	2	4	.912	.946	.973							
700-809	21.2	11.2	5.7	3.2	2.6	1.7	5.7	3.0	0.9	1.2	1.7											

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Handford formation: proportional mortality analysis, age for age 4 yrs. of death

Cause+ICD	TotP	NG	0-2	3-4	5-6	7-8	9-10	11-20	21-40	41-60	61-100	101+	E-NE R <sub>u</sub> /E	lim. dev. %	6 mt. R <sub>u</sub> /E	lim. E on cum. dev. of death
																-3 -5 -10 -15 -20
Supra. foss. du	5	4	0	1	0	0	0	0	0	0	0	0	.364 .143	.014 .156 .343		.215 .298 .327 .345
0-136		3.6	0.4	0.3	0.1	0.2	0.1	0.1	0.0	0.0	0.0	0.0				
all cancer	117	82	15	3	2	5	3	3	1	2	0	1	.365 .922	.291 .276 .940		.945 .928 .723 .743 .414
140-239		80.5	14.3	7.8	1.8	4.4	2.8	2.6	1.3	0.7	0.6	0.4				
ca dig. & rg	25	17	3	0	1	2	0	0	1	1	0	0	.586 .639	.643 .751 .877		.642 .24 .510 .715
150-159		17.5	2.9	1.4	0.5	1.0	0.5	0.5	0.3	0.2	0.2	0.0				
Ca lge. outst	16	12	1	0	0	2	0	0	0	1	0	0	.360 .730	.665 .844 .945		.677 .689 .723 .844
153		11.2	1.8	0.9	0.2	0.7	0.3	0.3	0.2	0.1	0.1	0.2				
ca. resp. syst	8	5	2	0	0	0	1	0	0	0	0	0	.575 .668	.031 .061 .317		.171 .112 .320 .174
160-163		5.3	1.0	0.6	0.1	0.3	0.2	0.2	0.0	0.0	0.0	0.1				
Ca. lung			same as ca. resp. system													
162			same as ca. resp. system													
ca. breast	29	21	3	2	0	1	0	1	0	0	0	1	.237 .851	.747 .635 .844		.869 .865 .544 .501 .762
174		19.6	3.5	2.1	0.4	1.1	0.8	0.8	0.3	0.2	0.1	0.1				
ca. cerv. uter.	7	4	2	0	0	0	0	1	0	0	0	0	.633 .341	.416 .20 .314		.339 .67 .101 .227
180		5.0	0.8	0.5	0.0	0.2	0.2	0.2	0.1	0.0	0.0	0.0				
ca. cerv. ut.	6	6	0	0	0	0	0	0	0	0	0	0	.066	///	///	///
182		4.3	0.4	0.4	0.1	0.3	0.2	0.1	0.0	0.1	0.0	0.0				
ca. cerv. body	13	12	1	0	0	1	1	0	0	0	0	0	.349 .495	.443 .659 .503		.498 .472 .425 .393
183		8.9	2.0	0.8	0.2	0.4	0.2	0.2	0.2	0.0	0.0	0.0				
ca. larynx. & tr.	10	9	0	0	1	0	0	0	0	0	0	0	.066 .460	.288 .477 .433		.474 .73 .5 .5
200-209		6.9	1.0	0.6	0.3	0.5	0.3	0.2	0.1	0.1	0.1	0.0				
endocerv. ut.	8	6	1	1	0	0	0	0	0	0	0	0	.442 .042	.00000 .036 .305		.108 .095 .20 .279
190-279		5.7	0.9	0.3	0.2	0.5	0.1	0.1	0.0	0.1	0.1	0.0				
Neurolog. Sancer	6	5	0	1	0	0	0	0	0	0	0	0	.281 .548	.496 .513 .366		.641 .022 .062 .021
320-399		4.2	0.8	0.2	0.3	0.3	0.0	0.0	0.0	0.1	0.1	0.0				
Sachm. H. D.	74	57	4	4	1	3	0	2	0	1	2	0	.057 .767	.569 .906 .897		.722 .726 .871 .550
410-414		52.0	6.9	3.8	2.4	3.7	2.1	1.2	0.3	1.0	0.6	0.2				
ca. tr. MI	42	36	3	1	1	3	0	2	0	1	1	0	.131 .750	.623 .825 .879		.661 .694 .676 .497
410-411		33.4	4.3	3.0	1.2	2.2	1.6	0.9	0.2	0.7	0.3	0.2				
Chronic MI	26	21	1	3	0	0	0	0	0	0	1	0	.194 .502	.434 .468 .596		.408 .422 .57 .475
412-414		18.5	2.5	0.8	1.2	1.5	0.4	0.3	0.1	0.4	0.3	0.1				
CVD	37	21	8	3	3	0	1	0	1	0	0	0	(.971) .150	.332 .062 .108		.157 .165 .143 .325
430-438		25.7	4.5	1.8	1.3	1.5	0.9	0.4	0.3	0.4	0.1	0.1				
Stom. Canc.	26	19	0	1	1	2	1	1	1	0	0	0				
440-449		17.9	2.8	1.9	0.3	1.1	0.7	0.7	0.2	0.2	0.2	0.1				
Resp. disease	13	9	2	2	0	0	0	0	0	0	0	0	.369 .225	.293 .216 .324		.307 .319 .317 .306
460-519		8.7	1.9	0.9	0.2	0.4	0.3	0.3	0.1	0.1	0.0	0.1				
Hg. dis.	24	14	4	0	3	3	0	0	0	0	0	0	.915 .308	.478 .423 .217		.311 .299 .263 .368
520-577		17.2	2.7	1.3	0.5	1.1	0.5	0.3	0.1	0.2	0.1	0.0				
Endometriosis	5	4	0	0	1	0	0	0	0	0	0	0	.278 .420	.364 .506 .448		.446 .452 .527 .763
580-629		3.4	0.6	0.3	0.1	0.2	0.1	0.1	0.1	0.0	0.0	0.0				
Fr. Fract.	24	18	2	2	0	1	0	1	0	0	0	0	.388 .436	.261 .440 .479		.425 .441 .353 .308
500-519		17.2	3.1	1.6	0.3	0.8	0.4	0.4	0.2	0.2	0.2	0.2				

Harford males; proportional mortality analysis, day for year

Cause + ICD	Total	cum. dose at death											E-NE lin/E	6-mth			11-ds.0 intervals					
		NE	0-2	3-4	5-6	7-8	9-10	11-20	21-40	41-60	61-100	101+		lin dose 1/4	lin/E	lin/E	lin/E	lin/E	lin/E	lin/E		
all cancer 140-239	698	245	123	82	45	33	27	59	40	12	12	20	.913	.775	.864	.912	.728	.642	.636	.914	.832	.6
ca. buccal cavity 140-149	23	9	6	1	3	1	0	2	0	0	0	1	.404	.479	.453	.253	.335	.515	.591	.257	.221	.6
ca. tongue 141	6	3	2	0	0	0	0	0	0	0	0	1	.143	.874	.791	.533	.143	.842	.877	.385	.435	.25
ca. dig. + perit. 150-159	213	67	39	30	17	13	4	20	11	4	2	6	.920	.613	.823	.697	.409	.525	.504	.724	.389	.63
ca. esophagus 150	18	9	2	4	2	0	0	0	1	0	0	0	.152	.240	.162	.228	.220	.255	.281	.316	.320	.2
ca. stomach 151	38	12	8	5	5	1	0	3	3	1	0	0	.847	.177	.286	.279	.122	.139	.155	.201	.179	.3
ca. large intest 153	63	13	13	12	2	5	3	6	6	1	1	1	.998	.300	.627	.499	.257	.373	.442	.790	.539	.4
ca. rect + RST 154	19	3	4	1	5	2	0	2	1	0	1	0	.984	.350	.615	.537	.543	.253	.181	.279	.421	.4
ca. liver 155	9	2	2	2	0	0	0	3	0	0	0	0	.830	.239	.344	.301	.202	.222	.210	.194	.234	.3
ca. gallbladder 156	10	7	2	0	0	1	0	0	0	0	0	0	.107	.329	.144	.253	.308	.330	.338	.376	.402	.26
ca. pancreas 157	51	19	7	6	2	3	1	6	0	2	0	5	.531	.999	.999	.992	.926	.996	.990	.978	.861	.95
ca. nasopharynx 160-163	207	69	32	23	11	9	12	23	11	4	8	5	.825	.722	.797	.943	.902	.603	.654	.790	.636	.152
ca. larynx 161	10	3	2	1	0	1	1	0	1	1	0	0	.590	.285	.314	.390	.175	.329	.372	.545	.615	.15
ca. lung 162	194	66	28	21	11	8	11	23	10	3	8	5	.775	.772	.821	.972	.958	.633	.702	.839	.702	.29
mediast. melanoma 172	11	2	5	0	1	2	0	0	1	0	0	0	.930	.161	.319	.111	.158	.208	.161	.226	.113	.15
ca. prostate 185	43	22	5	3	5	2	1	1	4	0	0	0	.022	.205	.084	.352	.167	.204	.195	.267	.208	.32
ca. testis 186	4	1	1	0	0	0	1	0	1	0	0	0	.684	.413	.472	.569	.474	.447	.499	.632	.607	.29
ca. bladder 188	11	4	0	2	1	1	0	1	2	0	0	0	.696	.479	.546	.797	.458	.303	.311	.354	.470	.15
ca. other urinary 189	23	8	4	2	2	1	3	2	0	0	0	1	.715	.745	.785	.652	.547	.803	.881	.986	.410	.12
ca. brain 191	21	7	2	3	0	1	2	1	2	1	0	2	.434	.912	.904	.908	.733	.809	.700	.551	.735	.9
ca. other nerv. 192	5	2	2	1	0	0	0	0	0	0	0	0	.391	.215	.201	.992	.185	.216	.222	.234	.244	.3
ca. all other 195	4	2	2	0	0	0	0	0	0	0	0	0	.282	.263	.299	.125	.201	.266	.296	.353	.093	.64