2. Internal Comparison Group

Based on these early results, there appears to be no significant difference between Ranch Handers and comparisons as regards mortality. This null finding holds for both cause specific and noncause specific comparisons. One within group comparison did yield a significant difference, however. The non-Black comparison officers are living significantly longer than the non-Black comparison enlisted personnel. This may reflect the underlying health care and socioeconomic differences between these two groups. Non-Black Ranch Hand officers also appear to be living longer than non-Black Ranch Hand enlisted personnel, but this finding cannot be viewed as significant, with a P-value of .142 (Table 17). This lack of significance in the Ranch Hand analysis might be attributed to the smaller group sizes within the Ranch Hand cohort in contrast to the comparison cohort.

3. External Comparisons

As outlined in the study protocol, considerable effort was expended in the selection of the study comparison group. While the chosen comparison group appeared closest to the Ranch Hand cohort except for herbicide exposure, it seemed appropriate to also contrast the Ranch Hand mortality experience to that of additional comparison groups. Three additional comparison data sets were then selected: mortality data from the West Point Class of 1956, the DoD Nondisability Retired Officer and Enlisted Life Tables for 1978, and the U.S. White Male Life Table, also for 1978. These data sets were chosen in a hierarchical fashion with the expectation that, in the absence of a herbicide effect, the Ranch Handers would have: 1) a mortality pattern comparable to the West Pointers, 2) a lower mortality than the DoD group due to the healthy worker effect, and 3) a still lower mortality than the U.S. male cohort due to healthy worker and military selection effects. These expectations were reassuringly fully realized with respect to overall mortality. Additionally, interesting officer-enlisted differentials emerged. As discussed below, these officer-enlisted differentials may have resulted from sample size effects or from covariable effects, potentially including herbicide exposure.

4. Power Considerations

The power limitations of this study, specifically regarding mortality from rare conditions, such as soft tissue sarcoma, were fully acknowledged and described in the protocol (Ref 1, page 67). For example, a fatal disease with an incidence of .001 would require an approximate risk of 4 for a power of 0.8.

Power calculations, while desirable for planning and study design, are also revealing at analysis. They are, however, sometimes difficult to carry out without further assumptions. The powers of the logrank and Wilcoxon tests

and the likelihood ratio tests in the SMR analyses are not calculable at this time due to the lack of appropriate methodology. The powers of the tests for cause specific mortality were calculated at the estimated relative risk. The values were low because the estimates of relative risk were close to unity and/or the data were sparse.

The null findings in this report are unlikely to have been observed by chance had the true group differences been substantial. For example, if the true overall relative risk were in fact equal to 2, a crude calculation gives a probability of .0007 of observing a relative risk smaller than the observed .964 (Table 7). This probability is less than .001 if the true relative risk is 1.5. These findings are, therefore, very likely reflective of a near overall equivalence between Ranch Handers and their matched comparisons. Finally, these unadjusted findings do not preclude the possibility of the emergence of significant differences after adjustment for risk factors.

5. Consistency Patterns

When the analysis of each external comparison data base is considered separately, the restrictions inherent in each source limit the strength of the inferences which can be made. However, when the results of all internal and external comparison data bases are considered in context, some patterns of consistency emerge. While some of these patterns may not have firm statistical underpinnings, they still may provide epidemiologic clues to the dynamics of the mortality process.

The Ranch Hand officers exhibit a very consistent and predictable pattern across all analyses. As shown in Table 43, their mortality is nearly the same as that of their most equivalent comparison groups (the matched comparison group officers and the West Point group). As the comparison groups become progressively less equivalent to the Ranch Hand group, the relative mortality of the Ranch Hand officers improves, presumably due to selection comparability (healthy worker effect, etc.). Their mortality is lower than that of their enlisted counterparts; however, this difference is not as striking as is the statistically significant comparable analysis between the matched comparison officers and the matched enlisted personnel.

Unfortunately, the cross-comparison trends for the enlisted Ranch Handers are not as clearcut. Their mortality is greater,though not significantly different from their matched comparisons. The enlisted comparison group had a highly significant underrepresentation of mortality against both the DoD and US life tables, whereas the Ranch Handers are equivalent to the DoD group and only marginally better than the 1978 US White males.

The consistent observation that the enlisted Ranch Handers appear to demonstrate less of a difference in relative mortality than do their matched comparisons is intriguing. This may reflect an actual increase in mortality due to herbicide exposure or some other factor, or it could be an artifact of small sample size created by the 1:5 matching or basic comparability problems as previously described. The inclusion of substantially more subjects in one group than another can have a profound effect on the significance level of a

statistical technique. Nevertheless, these observations are of interest, and will continue to be subjected to detailed analysis throughout the course of the follow-up study. This trend is consistent with self-perception of herbicide exposure held by many of the Ranch Hand group. Covariate analyses will be conducted, the herbicide exposure index will be applied to these data, and the effects of interaction will be assessed to determine whether the Ranch Hand enlisted findings are real or artifactual.

The next mortality assessment will include analyses by person-year of follow-up, adjusted for age in an effort to better address the issue of latency. As the number of deaths in the study population increases with the passage of time, all of the statistical approaches outlined in the protocol (1) will be applied to the data.

Appendix I

RANCH HAND II PRINCIPAL INVESTIGATORS
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Appendix II

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Appendix III

MATCHING RESULTS IN THE MORTALITY POPULATION

The matching results are described here for the mortality population consisting of 1241 Ranch Hands, their 6171 matched mortality comparisons, and the six unmatched Ranch Hands. The matching procedure is described in the Protocol (Ref. 1, pages 23-26).

All study subjects were matched perfectly on job category. Three mismatches occurred on race because the recorded race designations for three study subjects were found to be incorrect at the LHA interview. These three subjects were comparisons, two were in the enlisted-other stratum (one was originally recorded as Black and was discovered to be non-Black, the other was originally recorded as non-Black and was discovered to be Black), and one was in the enlisted-flight engineer stratum (he was originally recorded as Black and was discovered to be non-Black).

Matching on date of birth was carried out by first expressing date of birth in months from 1 January 1900, to the nearest month; the result is termed month-of-birth. Six discrepancies occurred in matching on month-of-birth due to erroneous months-of-birth for one Ranch Hand and one comparison. These were discovered at the LHA interview. The Ranch Hand, in the non-Black enlisted-other stratum, was discovered to be 72 months older than was recorded prior to the matching. The comparison, in the non-Black officer-pilot stratum, was found to be 15 years younger than was originally recorded. The erroneous Ranch Hand month-of-birth put all five of his matched comparisons 12 months out of range since he was originally perfectly matched to all five mortality comparisons. The erroneous comparison month-of-birth put that comparison 119 months out of range. Given the very small number of mismatches on age and race relative to the number of subjects, their effect was assumed negligible.

The matching by month-of-birth, overall, and within each of the ten job and race categories within the mortality population is summarized in this Appendix. The column headed "Age Difference" lists absolute differences of months-of-birth of Ranch Hands and comparisons. The column headed "Number of Comparisons with RH younger (older)" gives, at each level of age difference, the number of comparisons within the level of age difference and older (younger) than the Ranch Hand to whom they are matched. The column headed "Total Count" gives the total numbers of comparisons having the absolute age differences with their matched Ranch Hand given in the first column; in "Total Percent", these counts are expressed as percentages of 6171. These are cumulated in the last two columns.

Appendix III

MATCH SUMMARY FOR THE MORTALITY POPULATION

Strata	Age Difference	Number of Comparisons with RH Younger	Older	Total Count	%	Cumulative Total	%
Overall	0			4261	69.0	4261	69.0
	1-6	743	706	1449	23.5	5710	92.5
	7-12	77	102	179	2.9	5889	95.4
	13-18	40	36	76	1.2	5965	96.7
	19-24	22	22	44	0.7	6009	97.4
	25-30	12	19	31	0.5	6040	97.9
	31-36	16	14	30	0.5	6070	98.4
	37-42	10	19	29	0.5	6099	98.8
	43-48	9	13	22	0.4	6121	99.2
	49-54	13	7	20	0.3	6141	99.5
	55-60	17	7	24	0.4	6165	99.9
	72	0	5	5	0.1	6170	100.0
	179	0	1	1	0.0	6171	100.0
Officer-pilot	0			961	55.2	961	55.2
Non-Black	1-6	272	259	531	30.5	1492	85.8
	7-12	33	32	65	3.7	1557	89.5
	13-18	20	17	37	2.1	1594	91.6
	19-24	8	12	20	1.1	1614	92.8
	25-30	9	11	20	1.1	1634	93.9
	31-36	13	10	23	1.3	1657	95.2
	37-42	7	18	25	1.4	1682	96.7
	43-48	7	11	18	1.0	1700	97.7
	49-54	11	7	18	1.0	1718	98.7
	55-60	14	7	21	1.2	1739	99.9
	179	0	1	1	0.1	1740	100.0
Officer-Pilot	0			0	0.0	0	0.0
Black	1-6	3	0	3	23.1	3	23.1
	7-12	3	0	3	23.1	6	46.2
	31-36	0	1	1	7.7	7	53.9
	37-42	2	0	2	15.4	9	69.2
	43-48	1	0	1	7.7	10	76.9
	49-54	2	0	2	15.4	12	92.3
	55	1	0	1	7.7	13	100.0
Officer-	0			240	61.5	240	61.5
Navigator	1-6	74	70	144	36.9	384	98.5
Non-Black	7-12	0	6	6	1.5	390	100.0

Appendix III (Continued)
MATCH SUMMARY FOR THE MORTALITY POPULATION

Strata	Age Difference	Number of Comparisons with RH Younger	Older	Total Count	%	Cumulative Total	%
Officer-Navigator Black	0			1	10.0	1	10.0
	1-6	0	1	1	10.0	2	20.0
	7-12	2	2	4	40.0	6	60.0
	13-18	0	1	1	10.0	7	70.0
	19-24	0	1	1	10.0	8	80.0
	25-30	0	1	1	10.0	9	90.0
	31-36	0	1	1	10.0	10	100.0
Officer-Other Non-Black	0			14	11.4	14	11.4
	1-6	38	57	95	77.2	109	88.6
	7-12	2	8	10	8.1	119	96.8
	13-18	1	1	2	1.6	121	98.4
	19-24	1	0	1	0.8	122	99.2
	25	0	1	1	0.8	123	100.0
Officer-Other Black	13-18	2	0	2	100.0	2	100.0
Enlisted-Flight Engineer Non-Black	0			516	55.2	516	55.2
	1-6	165	141	306	32.7	822	87.9
	7-12	29	34	63	6.7	885	94.7
	13-18	16	14	30	3.2	915	97.9
	19-24	0	7	7	0.7	922	98.6
	25-30	2	6	8	0.9	930	99.5
	31-36	2	1	3	0.3	933	99.8
	37-42	1	0	1	0.1	934	99.9
	46	1	0	1	0.1	935	100.0
Enlisted-Flight Engineer Black	0			10	13.3	10	13.3
	1-6	26	22	48	64.0	58	77.3
	7-12	7	5	12	16.0	70	93.3
	19-24	3	0	3	4.0	73	97.3
	55-58	2	0	2	2.7	75	100.0
Enlisted-Other Non-Black	0			2382	90.6	2382	90.6
	1-6	116	91	207	7.9	2589	98.5
	7-12	1	11	12	0.5	2601	99.0
	13-18	1	3	4	0.2	2605	99.1
	19-24	10	2	12	0.5	2617	99.6
	25-30	1	0	1	0.0	2618	99.6
	31-36	1	1	2	0.1	2620	99.7
	37-42	0	1	1	0.0	2621	99.7
	43-48	0	2	2	0.1	2623	99.8
	72	0	5	5	0.2	2628	100.0
Enlisted-Other Black	0			137	53.7	137	53.7
	1-6	49	65	114	44.7	251	98.4
	7-12	0	4	4	1.6	255	100.0

Appendix IV

YEAR OF BIRTH, OCCUPATIONAL AND RACE SPECIFIC MORTALITY

Job Category, Race	Birth Year	Ranch Hand At Risk	Ranch Hand Dead	Ranch Hand Death Rate	Comparison At Risk	Comparison Dead	Comparison Death Rate
Officer-Pilot, Non-Black	1915-19	8	3	.375	39	4	.103
	1920-24	31	0		155	13	.084
	1925-29	31	0		232	14	.060
	1930-34	113	3	.027	456	23	.050
	1935-39	66	3	.045	326	8	.025
	1940-44	60	1	.017	354	5	.014
	1945-49	40	2	.050	178	5	.028
	TOTAL	349	12	.034	1740	72	.041
Officer-Pilot, Black	1930-34	0	0		3	0	
	1935-39	1	0		4	0	
	1940-44	3	0		6	0	
	1945-49	2	0		0	0	
	TOTAL	6	0		13	0	
Officer-Navigator Non-Black	1925-29	9	0		47	3	.064
	1930-34	35	1	.029	163	7	.043
	1935-39	21	1	.048	105	3	.029
	1940-44	13	0		67	0	
	1945-49	2	0		8	0	
	TOTAL	80	2	.025	390	13	.033
Officer-Navigator Black	1930-34	1	0		6	0	
	1935-39	1	0		4	0	
	TOTAL	2	0		10	0	
Officer-Other, Non-Black	1910-14	1	0		2	0	
	1915-19	0	0		3	0	
	1920-24	1	0		6	0	
	1925-29	3	0		11	1	.091
	1930-34	2	0		12	1	.083
	1935-39	4	0		19	0	
	1940-44	13	1	.077	66	1	.015
	1945-49	1	0		4	0	
	TOTAL	25	1	.040	123	3	.024

Appendix IV (Continued)

Job Category, Race	Birth Year	Ranch Hand At Risk	Ranch Hand Dead	Death Rate	Comparison At Risk	Comparison Dead	Death Rate
Officer-Other, Black	1940-44	1	0		2	0	
	TOTAL	1	0		2	0	
Enlisted-Flt Eng Non-Black	1915-19	1	1	1.000	6	2	.333
	1920-24	4	0		20	4	.200
	1925-29	12	0		61	3	.049
	1930-34	64	3	.047	304	15	.049
	1935-39	48	2	.042	243	10	.041
	1940-44	41	0		211	7	.033
	1945-49	19	0		90	5	.056
	TOTAL	189	6	.032	935	46	.049
Enlisted-Flt Eng Black	1925-29	1	0		10	1	.100
	1930-34	6	1	.167	34	5	.150
	1935-39	5	0		16	1	.063
	1940-44	3	1	.333	15	2	.133
	TOTAL	15	2	.133	75	9	.120
Enlisted-Other Non-Black	1905- 9	0	0		2	0	
	1910-14	4	2	.500	10	2	.200
	1915-19	8	0		48	5	.104
	1920-24	12	3	.250	60	7	.117
	1925-29	28	2	.071	140	18	.129
	1930-34	76	6	.079	376	14	.037
	1935-39	52	1	.019	263	8	.030
	1940-44	67	2	.030	340	7	.021
	1945-49	270	9	.033	1333	36	.027
	1950-54	11	0		56	0	
	TOTAL	528	25	.047	2628	97	.037
Enlisted-Other Black	1930-34	7	1	.143	35	2	.057
	1935-39	9	0		40	3	.075
	1940-44	7	0		35	1	.029
	1945-49	29	1	.034	145	4	.028
	TOTAL	52	2	.038	255	10	.039

Appendix V

THE EXTENDED EJIGOU-McHUGH RELATIVE RISK ESTIMATOR

Let R_k, k=1,2, ..., K, denote the distinct numbers of comparisons matched to the cases and let n_k denote the number of matched sets with exactly R_k comparisons. A matched set is defined as the case and his matched comparisons. Let $n=n_1+n_2+ \ldots +n_K$ denote the total number of matched sets.

Define $Z_{k,i,T}$, k=1,2, ...,K, i=0,1, by

$Z_{k,0,T}$ = the number of matched sets, among those having exactly R_k comparisons, in which the case is alive and exactly T of the R_k comparisons have died, T=1,2, ..., R_k

$Z_{k,1,T}$ = the number of matched sets, among those having exactly R_k comparisons in which the case has died and exactly T of the R_k comparisons have died, T=0,1,2, ..., R_k-1.

The extended estimate, ψ, is given by

$$\psi = \frac{\sum_{k=1}^{K}\sum_{T=1}^{R_k} Z_{k,0,T}Z_{k,1,T-1}/(Z_{k,0,T}+Z_{k,1,T-1})}{\sum_{k=1}^{K}\sum_{T=1}^{R_k} TZ^2_{k,0,T}/(R_k-T+1)(Z_{k,0,T}+Z_{k,1,T-1})}$$

and its variance is estimated by

$$\sigma^2 = \frac{\psi}{\sum_{k=1}^{K}\sum_{T=1}^{R_k} Z_{k,0,T}/[\psi+(R_k-T+1)/T]}.$$

Since K is finite, this estimate has the same distributional properties as the Ejigou-McHugh estimator; it is asymptotically efficient and unbiased. The underlying assumptions used in its derivation are that the disease under study is of low incidence and that relative risk is constant over the levels of the matching variables. The Ejigou-McHugh estimate and the above extension are equivalent in asymptotic efficiency to maximum likelihood estimation (12).

Figure 4
SURVIVAL CURVE ESTIMATE AND 95% CONFIDENCE BANDS
FOR POOLED RANCH HANDERS

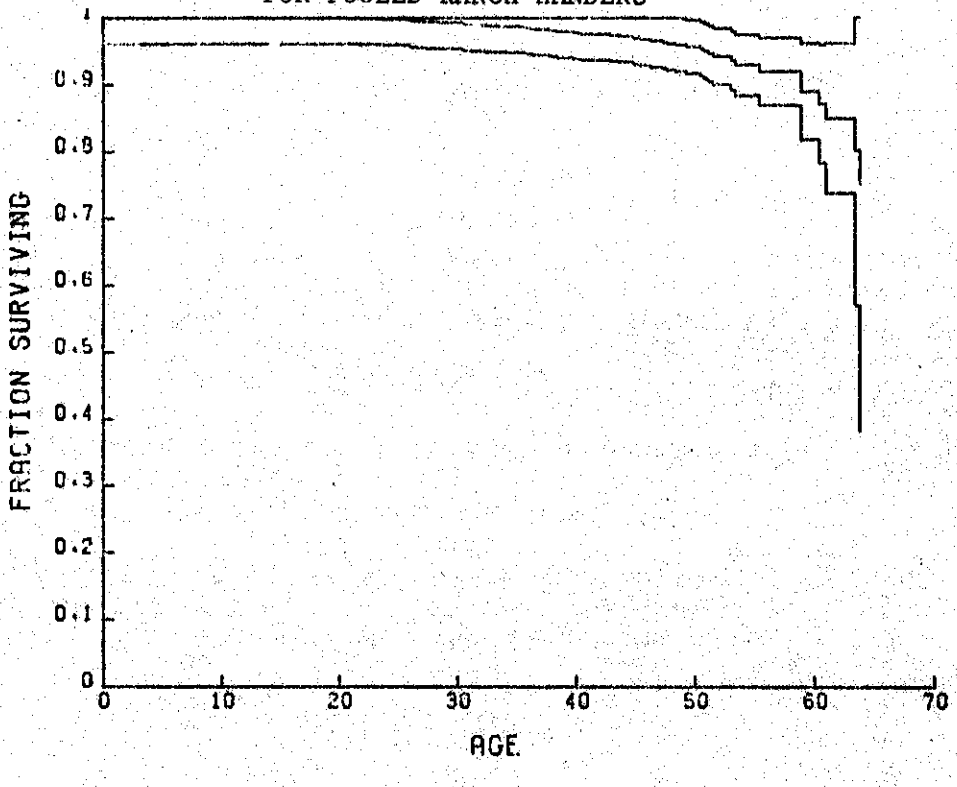


Figure 5
SURVIVAL CURVE ESTIMATE AND 95% CONFIDENCE BANDS
FOR POOLED COMPARISONS

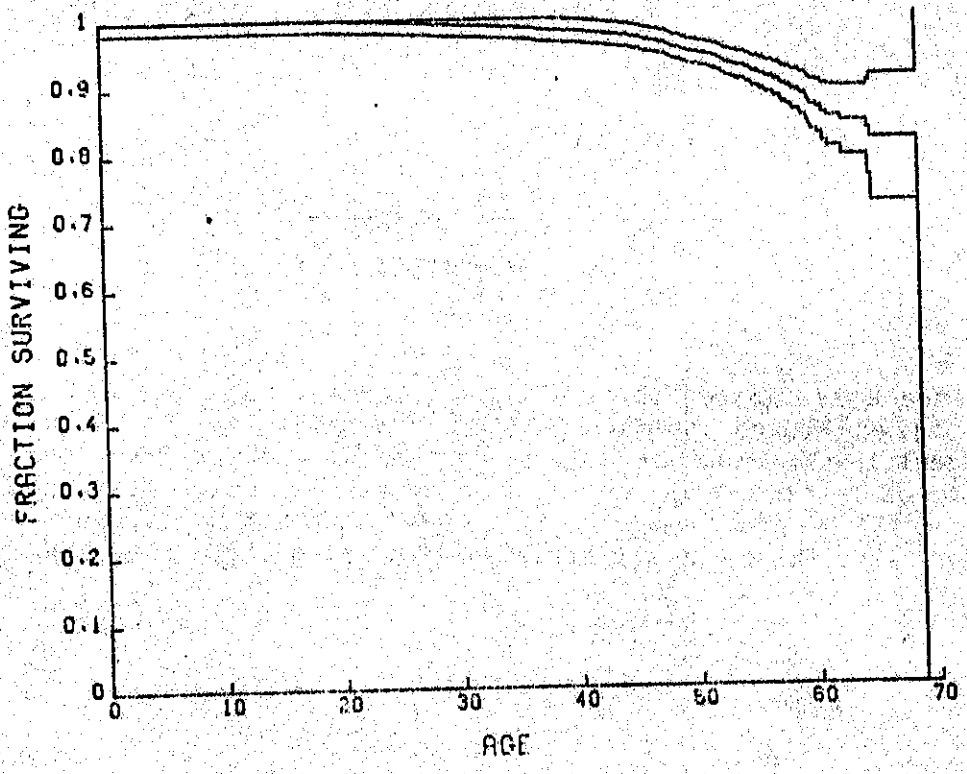


Figure 6
SURVIVAL CURVE ESTIMATE AND 95% CONFIDENCE BANDS
FOR RANCH HAND OFFICERS

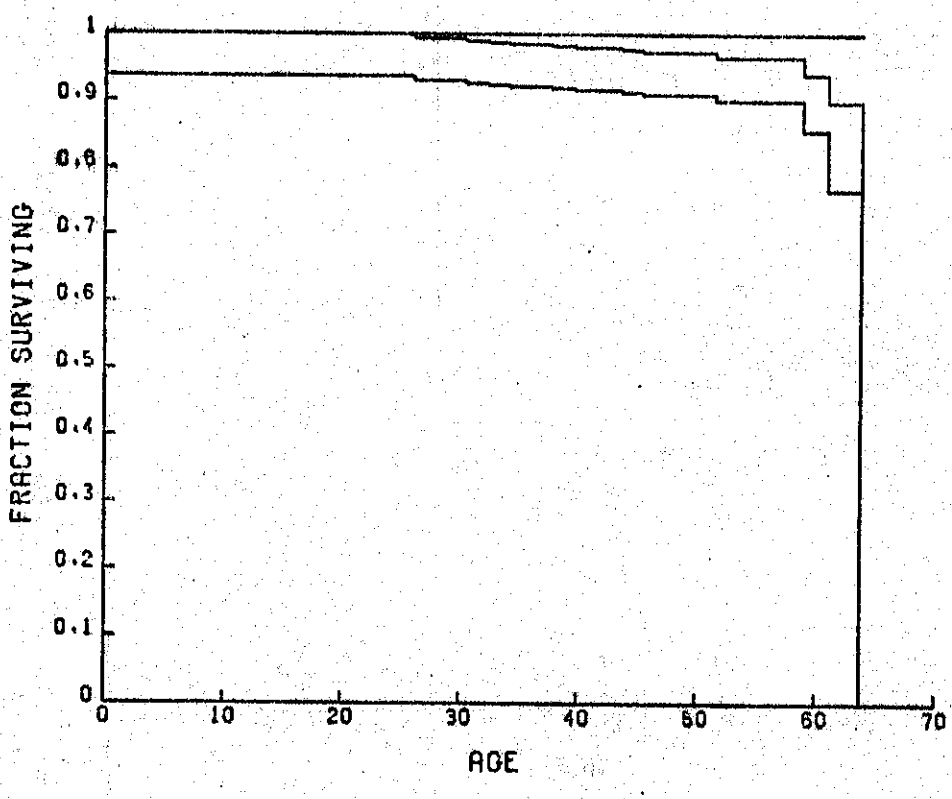


Figure 7
SURVIVAL CURVE ESTIMATE AND 95% CONFIDENCE BANDS
FOR COMPARISON OFFICERS

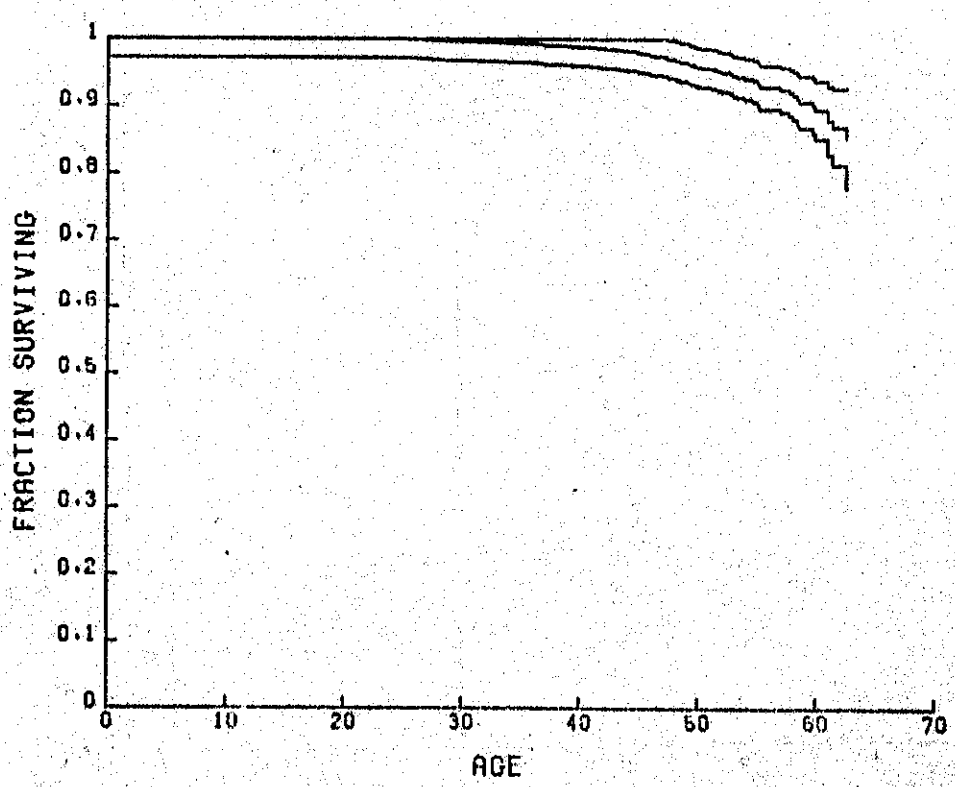


Figure 8

SURVIVAL CURVE ESTIMATE AND 95% CONFIDENCE BANDS
FOR RANCH HAND ENLISTED PERSONNEL

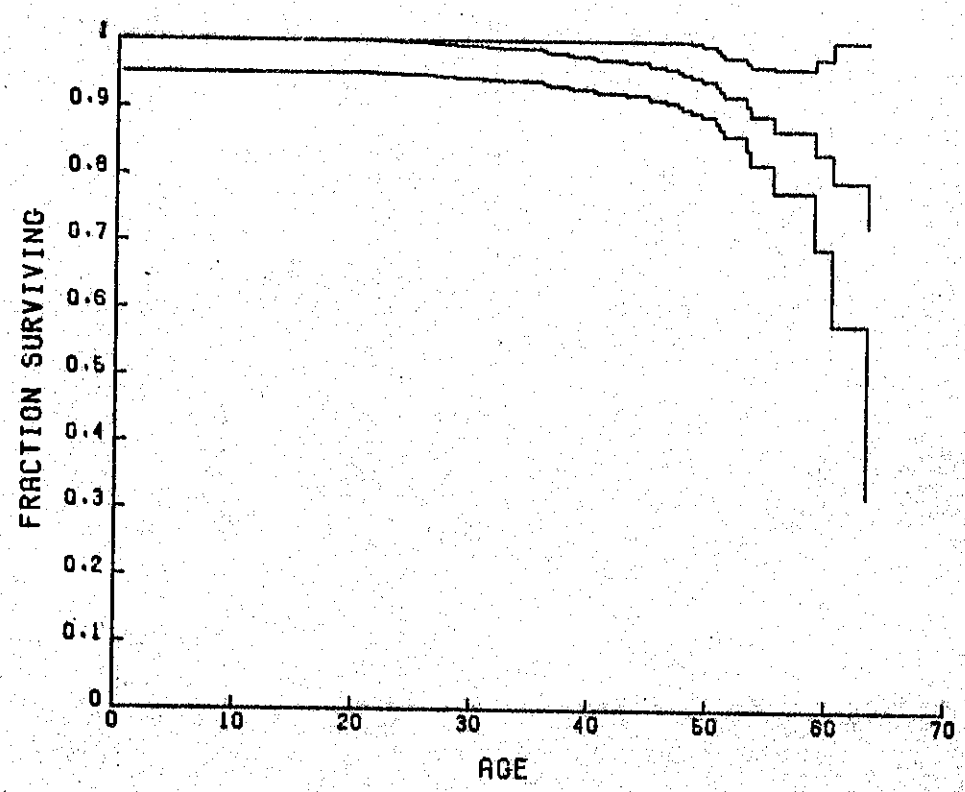


Figure 9

SURVIVAL CURVE ESTIMATE AND 95% CONFIDENCE BANDS
FOR COMPARISON ENLISTED PERSONNEL

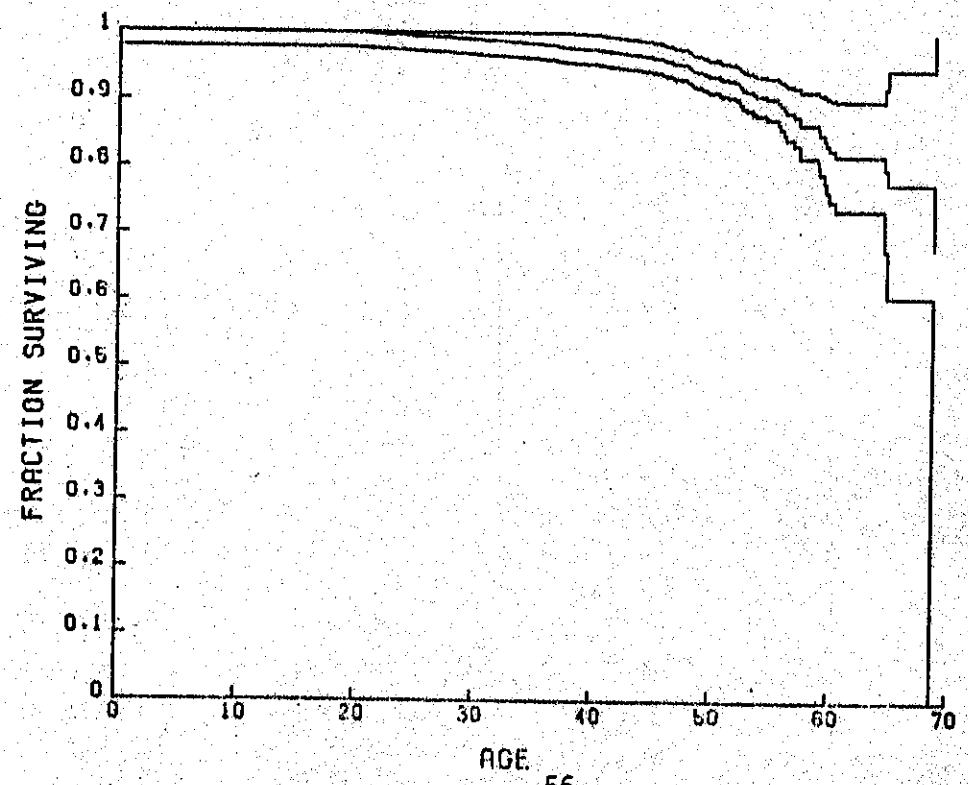


Figure 10

SURVIVAL CURVE ESTIMATE AND 95% CONFIDENCE BANDS
FOR RANCH HAND FLYING PERSONNEL

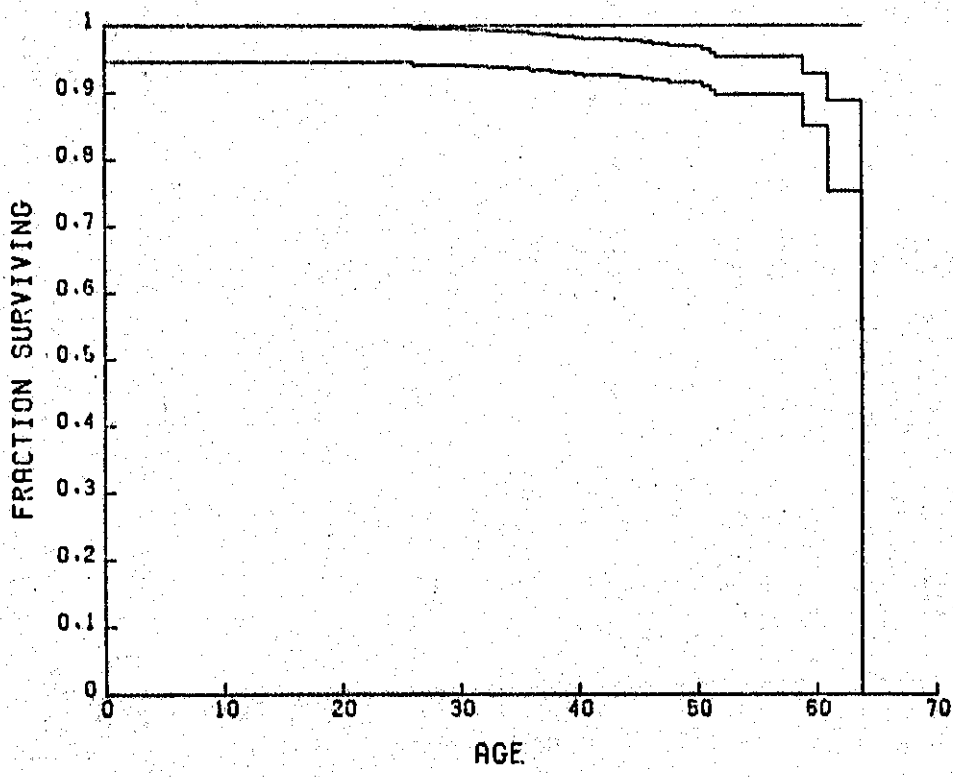


Figure 11

SURVIVAL CURVE ESTIMATE AND 95% CONFIDENCE BANDS
FOR COMPARISON FLYING PERSONNEL

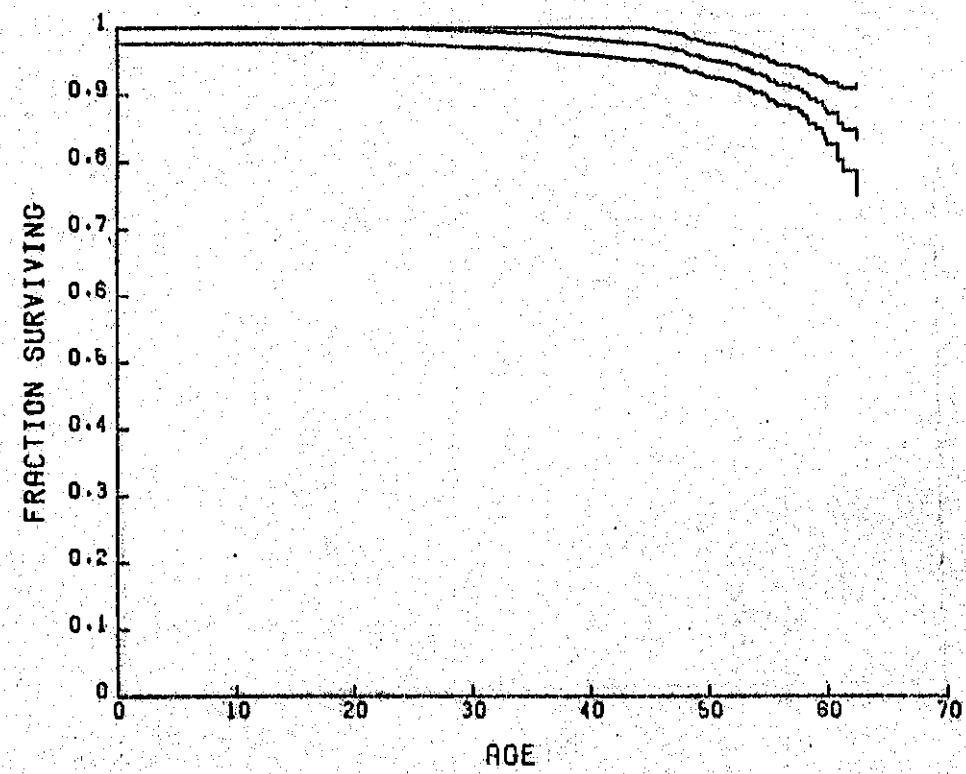


Figure 12

SURVIVAL CURVE ESTIMATE AND 95% CONFIDENCE BANDS
FOR RANCH HAND GROUND PERSONNEL

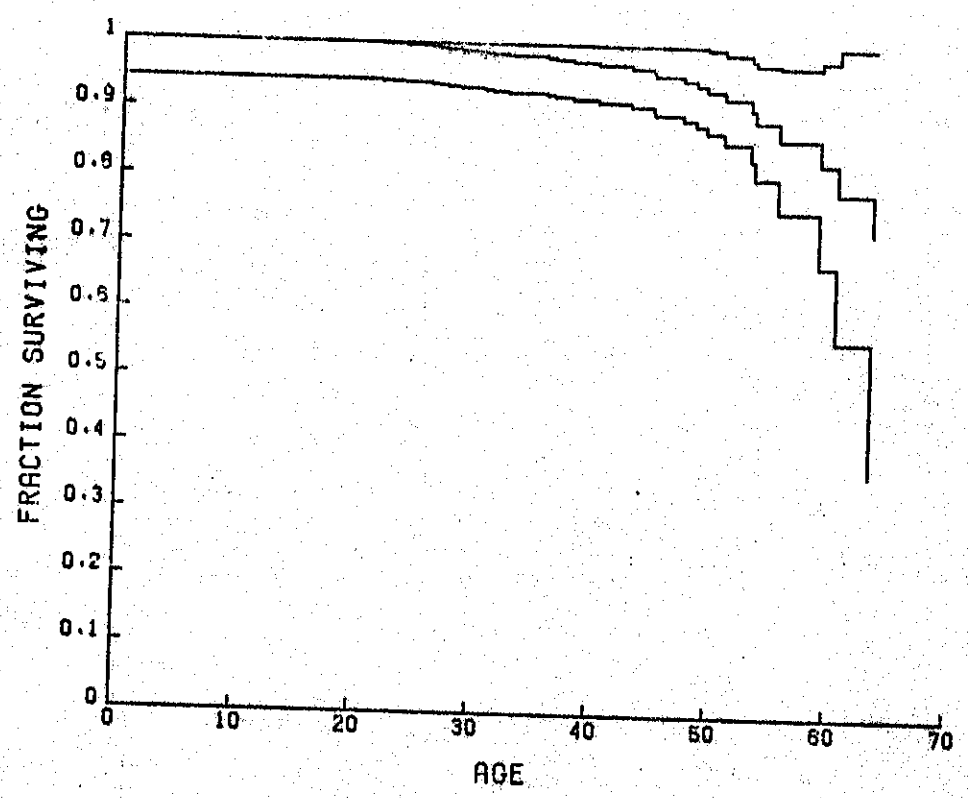
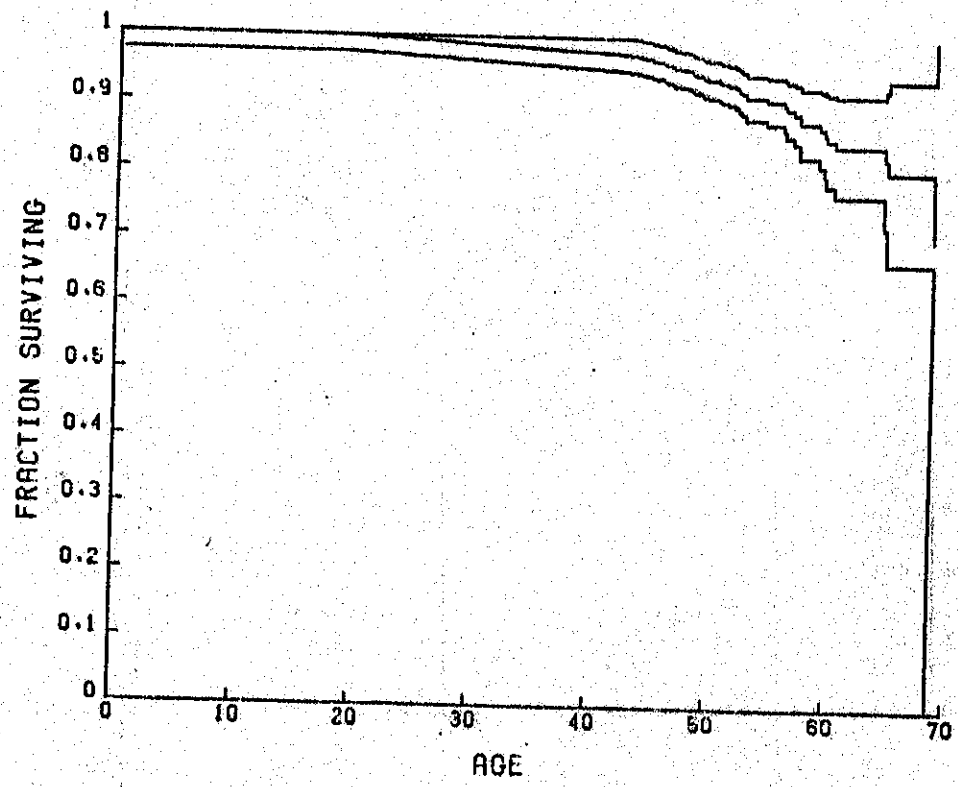


Figure 13

SURVIVAL CURVE ESTIMATE AND 95% CONFIDENCE BANDS
FOR COMPARISON GROUND PERSONNEL



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