

Chapter III

RANCH HAND VERSUS COMPARISON GROUP ANALYSES

1. Introduction

Overall survival comparisons, without regard to cause of death, were made via survival curve estimation, linear rank procedures, relative risk estimation and standardized mortality ratios. Survival curves were estimated and plotted using the method of Kaplan and Meier (6); 95% confidence bands (7) for each survival curve estimate were also plotted on each graph. Linear rank testing was carried out using the logrank test and Prentice's censored data extension of the Wilcoxon test (8). All linear rank tests were carried out with matched sets merged when Ranch Hands differed by less than one year relative to date of birth, within each stratum of job and race (9). These merged matched sets were regarded as separate strata for testing purposes (9, 10, 11). Relative risk estimates and confidence intervals were computed using an extension of the method of Ejigou and McHugh (12) to variable length, one-to-many matched sets (see Appendix V). Here, due to the one-to-many limitation of the algorithm, matched sets were not merged as when testing procedures were performed. Standardized mortality ratios and associated tests and plots were carried out as in Gail (13).

These analyses are fully adjusted for the matching variables, age, race and occupation, but are unadjusted for other variables of interest, such as length of time in Vietnam or Southeast Asia, herbicide dose, time since exposure, time in active duty military, and other medical or occupational risk factors. Some of these variables, such as herbicide dose and time since exposure will be adjusted for in the next analyses, after such data become available. In particular, latency analyses cannot be undertaken at this time but will be included in the next mortality report.

In these analyses, we have used summary statistics for which underlying modeling assumptions can be tested. For this reason, we have used the Breslow-Day (13) approach to SMR calculation, rather than the more traditional person-years method. A detailed explanation of this choice is given in Chapter VI.

2. Overall Comparisons

Survival time in these analyses was regarded as independent of censorship, if any, and was taken to be age at death. All subjects not certifiably dead, as of 31 December 1982, at the time of analysis, were considered censored at their age on that date. Contact has been lost with two Ranch Handlers and nine comparisons as described in Chapter II, but these are not assumed lost to follow-up for the purpose of mortality determination. They are assumed to have been alive on 31 December 1982. With this assumption, no subjects were lost to mortality follow-up before 31 December 1982 in this study.

Ranch Hand and comparison group survival curve estimates and their associated 95% confidence bands are shown in Figure 3 and Appendix VI for the five groups: pooled, officers, enlisted, flying and ground personnel, as defined in Table 4. The curves for the pooled groups are shown in Figure 3 with the 95% confidence interval bands deleted in the interest of legibility, but they are included in the group specific curves in Appendix VI. Review of

Ranch Hand operations has strongly suggested that Ranch Hand enlisted personnel were more heavily exposed to herbicide than Ranch Hand officers. Further, there is a perception of possible exposure differential between flying and ground Ranch Hand personnel. These notions prompted the above groupings and analyses seen in this and subsequent chapters. Analyses of latency are not possible at this time due to the as yet incomplete nature of the military service data base. These analyses will be performed after the hand review of military tour records has been completed.

Figure 3

SURVIVAL CURVE ESTIMATES FOR POOLED RANCH HANDERS AND COMPARISON SUBJECTS

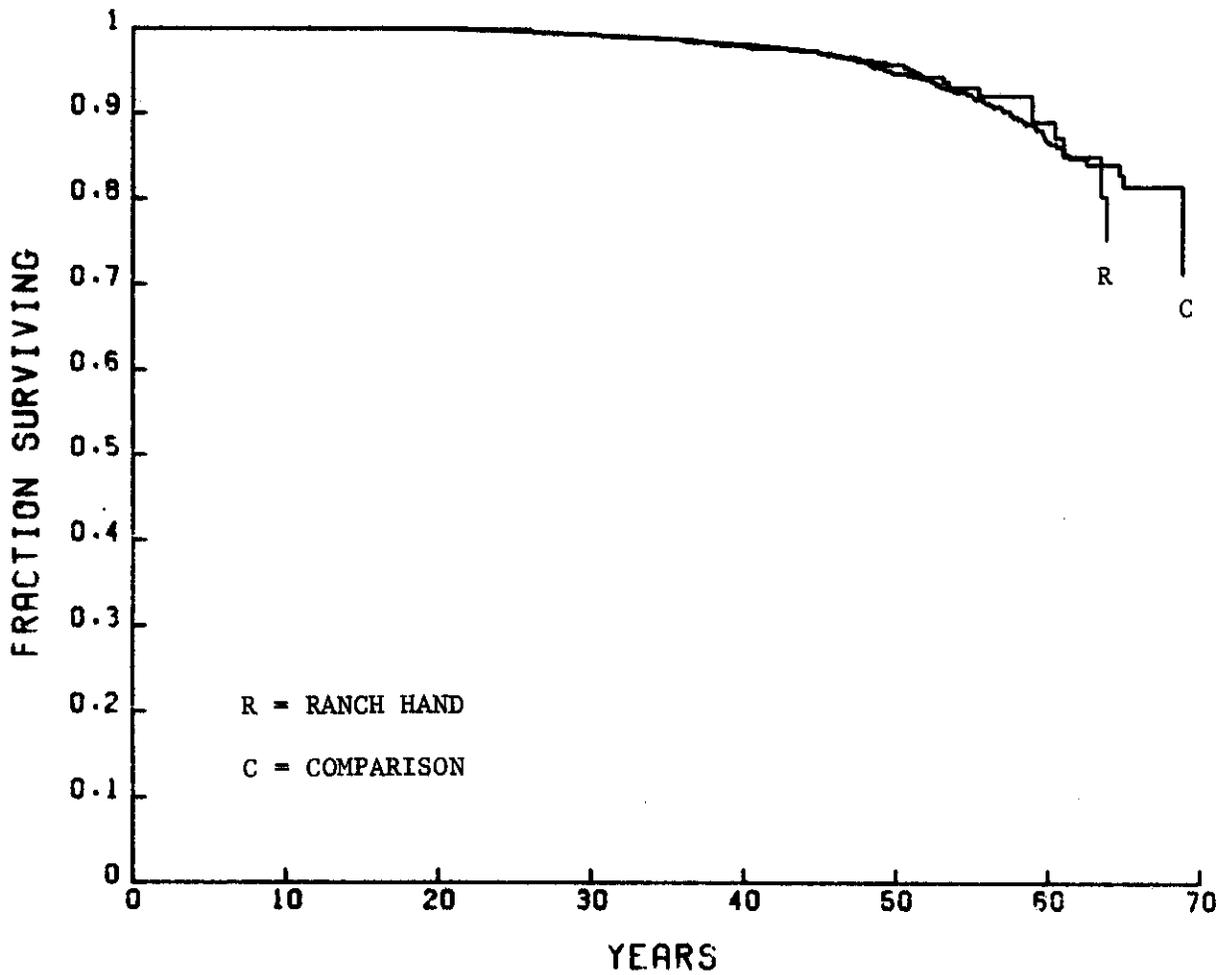


Table 4

GROUP DEFINITIONS

<u>Group</u>	<u>Definition</u>
Officer Enlisted	Officer-pilot, navigator, other Enlisted-flight engineer, other
Flying	Officer-pilot, navigator Enlisted-flight engineer
Ground	Officer-other Enlisted-other
Pooled	All occupational categories

Summary counts by group are shown in Table 5. Ignoring the matching, interaction between officer-enlisted categories and Ranch Hand membership, and interaction between flying-ground categories and Ranch Hand membership was evaluated using log-linear models. No statistically significant interactions were detected.

Table 5

SUMMARY COUNTS BY GROUP

<u>Group</u>	<u>Ranch Hand</u>			<u>Comparisons</u>		
	<u>At Risk</u>	<u>Dead</u>	<u>Rate</u>	<u>At Risk</u>	<u>Dead</u>	<u>Rate</u>
Officer	463	15	.032	2278	88	.039
Enlisted	784	35	.045	3893	162	.042
Flying	641	22	.034	3163	140	.044
Ground	606	28	.046	3008	110	.037
Pooled	1247	50	.040	6171	250	.041

Linear rank procedures were carried out on the same five groups. The results, summarized by test statistics and two-sided P-values, are shown in Table 6. Small P-values, less than .05, indicate significant differences, at the 5% level, between the two groups. These procedures are designed so that the statistic will be positive when the Ranch Handers are dying before the comparison subjects and negative when the comparisons are dying prior to the Ranch Handers. The null hypothesis is that the actual survival distributions of Ranch Handers and their matched comparisons are identical. Each statistic is approximately null distributed as a standard normal random deviate.

Table 6

TEST RESULTS AND P-VALUES FOR OVERALL COMPARISONS

<u>Group</u>	<u>Logrank</u>		<u>Wilcoxon</u>	
	<u>(Value)</u>	<u>P-Value</u>	<u>(Value)</u>	<u>P-Value</u>
Officer	(-0.634)	.526	(-0.722)	.470
Enlisted	(0.383)	.702	(0.331)	.741
Flying	(-1.021)	.307	(-1.116)	.264
Ground	(1.023)	.306	(0.950)	.342
Pooled	(-0.047)	.962	(-0.123)	.902

There is no significant difference, based on these data, between the Ranch Handers and their mortality comparison group. This means that, in particular, the mean ages-at-death of the Ranch Handers and their matched comparisons are not significantly different. In some groups, pooled, officer and flying, the statistics are negative, indicating that the Ranch Handers are living longer than the comparisons, but the differences are, again, insignificant, as evidenced by the large P-values. The situation is reversed for enlisted and ground personnel. These findings are consistent with the observation that, within each group, the comparison confidence bands are contained within the Ranch Hand confidence bands. When matched sets are stratified by five year intervals on year of birth, the same procedures give larger P-values than those in Table 6.

Relative risk estimates, the associated 95% confidence intervals, two-sided P-values for testing the null hypothesis of relative risk equal to unity and the associated power are given in Table 7. Here, the power of the test is defined as the conditional probability of rejecting the null hypothesis at the 5% level of significance, given that the relative risk is equal to its estimated value.

Table 7

RELATIVE RISKS AND 95% CONFIDENCE INTERVALS, P-VALUES AND POWER

<u>Group</u>	<u>Relative Risk</u>	<u>95% Confidence Interval</u>	<u>P-Value</u>	<u>Power</u>
Officer	0.763	(.320 - 1.207)	.373	.105
Enlisted	1.065	(.660 - 1.471)	.742	.072
Flying	0.734	(.387 - 1.081)	.211	.197
Ground	1.232	(.694 - 1.769)	.337	.195
Pooled	0.964	(.658 - 1.269)	.819	.051

The confidence intervals and P-values in Table 7 indicate no significant difference, at the 5% level, between the mortality of the Ranch Handers and comparisons in each of the five groups.

Year-of-birth specific mortality rates for each of the five groups are given in Tables 8 through 12, with the corresponding standardized mortality ratios (SMR). In each group, the comparisons are the internal standard. The SMR estimates relative risk in these comparisons if the year-of-birth specific relative risks are all equal (13). A likelihood ratio test for the hypothesis of equal year-of-birth specific relative risks was carried out for each comparison; its P-value is denoted by P1. In addition, the hypothesis that relative risk is unity, given that relative risk is constant across strata, was tested via a likelihood ratio procedure (13); its P-value is denoted by P2. The SMR and both P-values are given with each comparison.

Here, and elsewhere in this report, the denominator of the SMR is $\sum n_{ij}r_i$, where n_{ij} is the number of individuals for the i th stratum of the j th population and r_i is the death rate, per person, in the standard population for the i th stratum. In these calculations the data is stratified on year of birth.

Table 8

POOLED SPECIFIC MORTALITY RATES BY YEAR OF BIRTH
(SMR = .996; P1=.389, P2=.955)

Birth Year	Ranch Handers			Comparison		
	At Risk	Dead	Rate	At Risk	Dead	Rate
1905-14	5	2	.400	14	2	.143
1915-19	17	4	.235	96	11	.115
1920-24	48	3	.063	241	24	.100
1925-29	84	2	.024	501	40	.080
1930-34	304	15	.049	1389	67	.048
1935-39	207	7	.034	1020	33	.032
1940-44	208	5	.024	1096	23	.021
1945-54	374	12	.032	1814	50	.028
		50			250	

Table 9

OFFICER SPECIFIC MORTALITY RATES BY YEAR OF BIRTH
(SMR = .827; P1=.233, P2=.490)

Birth Year	Ranch Hand Officers			Comparison Officers		
	At Risk	Dead	Rate	At Risk	Dead	Rate
1910-24	41	3	.073	205	17	.083
1925-34	194	4	.021	930	49	.053
1935-39	93	4	.043	458	11	.024
1940-44	90	2	.022	495	6	.012
1945-49	45	2	.044	190	5	.026
		<u>15</u>			<u>88</u>	

Table 10

ENLISTED SPECIFIC MORTALITY RATES BY YEAR OF BIRTH
(SMR = 1.074; P1=.733, P2=.722)

Birth Year	Enlisted Ranch Handers			Enlisted Comparisons		
	At Risk	Dead	Rate	At Risk	Dead	Rate
1905-14	4	2	.500	12	2	.167
1915-19	9	1	.111	54	7	.130
1920-24	16	3	.188	80	11	.138
1925-29	41	2	.049	211	22	.104
1930-34	153	11	.072	749	36	.048
1935-39	114	3	.026	562	22	.039
1940-44	118	3	.025	601	17	.028
1945-54	329	10	.030	1624	45	.028
		<u>35</u>			<u>162</u>	

Table 11

FLYING SPECIFIC MORTALITY RATES BY YEAR OF BIRTH
(SMR = .769; P1=.678, P2=.238)

Birth Year	Flying Ranch Handers			Flying Comparisons		
	At Risk	Dead	Rate	At Risk	Dead	Rate
1915-24	44	4	.091	220	23	.105
1925-34	272	8	.029	1316	71	.054
1935-39	142	6	.042	698	22	.032
1940-44	120	2	.017	653	14	.021
1945-49	63	2	.032	276	10	.036
		<u>22</u>			<u>140</u>	

Table 12

GROUND SPECIFIC MORTALITY RATES BY YEAR OF BIRTH
(SMR = 1.257; P1=.535, P2=.302)

Birth Year	Ground Ranch Handers			Ground Comparisons		
	At Risk	Dead	Rate	At Risk	Dead	Rate
1905-14	5	2	.400	14	2	.143
1915-24	21	3	.143	117	12	.103
1925-29	31	2	.065	151	19	.126
1930-34	85	7	.082	423	17	.040
1935-39	65	1	.015	322	11	.034
1940-44	88	3	.034	443	9	.020
1945-54	311	10	.032	1538	40	.026
		<u>28</u>			<u>110</u>	

These SMR comparisons are in agreement with the preceding relative risk and linear rank analyses; there is no significant difference in mortality, based on these data, between the Ranch Hand group and the comparison group.

3. Noncause Specific Occupational Comparisons

Within-group comparisons by occupation via SMR's, with P-values for testing constant relative risk across year of birth strata (P1) and for testing relative risk equal to unity (P2) are given in Tables 13 through 16. The enlisted and ground personnel are the internal standards in these comparisons. Comparisons via the logrank procedure are given in Table 17.

Table 13

RANCH HAND OFFICERS VERSUS RANCH HAND ENLISTED
MORTALITY BY YEAR OF BIRTH
(SMR = .544; P1=.280, P2= .087)

Birth Year	Ranch Hand Officers			Ranch Hand Enlisted		
	At risk	Dead	Rate	At Risk	Dead	Rate
1905-24	41	3	.073	29	6	.207
1925-34	194	4	.021	194	13	.067
1935-39	93	4	.043	114	3	.026
1940-44	90	2	.022	118	3	.025
1945-54	45	2	.044	329	10	.030
		<u>15</u>			<u>35</u>	

Table 14

RANCH HAND FLYING PERSONNEL VERSUS RANCH HAND GROUND PERSONNEL
MORTALITY BY YEAR OF BIRTH
(SMR = .581; P1=.382, P2=.100)

Birth Year	Ranch Hand Fliers			Ranch Hand Ground		
	At Risk	Dead	Rate	At Risk	Dead	Rate
1905-24	44	4	.091	26	5	.192
1925-34	272	8	.029	116	9	.078
1935-39	142	6	.042	65	1	.015
1940-44	120	2	.017	88	3	.034
1945-54	63	2	.032	311	10	.032
		<u>22</u>			<u>28</u>	

Table 15

COMPARISON GROUP OFFICERS VERSUS COMPARISON GROUP ENLISTED
MORTALITY BY YEAR OF BIRTH
(SMR = .697; P1=.640, P2=.015)

Birth Year	Comparison Officers			Comparison Enlisted		
	At Risk	Dead	Rate	At Risk	Dead	Rate
1905-19	44	4	.091	66	9	.136
1920-24	161	13	.081	80	11	.138
1925-29	290	18	.062	211	22	.104
1930-34	640	31	.048	749	36	.048
1935-39	458	11	.024	562	22	.039
1940-44	495	6	.012	601	17	.028
1945-54	190	5	.026	1624	45	.028
		<u>88</u>			<u>162</u>	

Table 16

COMPARISON FLYING PERSONNEL VERSUS COMPARISON GROUND
MORTALITY BY YEAR OF BIRTH
(SMR = .930; P1=.305, P2=.867)

Birth Year	Comparison Fliers			Comparison Ground		
	At Risk	Dead	Rate	At Risk	Dead	Rate
1905-19	45	6	.133	65	7	.108
1920-24	175	17	.097	66	7	.106
1925-29	350	21	.060	151	19	.126
1930-34	966	50	.052	423	17	.040
1935-39	698	22	.032	322	11	.034
1940-44	653	14	.021	443	9	.020
1945-54	276	10	.036	1538	40	.026
		<u>140</u>			<u>110</u>	

Table 17

LOGRANK WITHIN GROUP COMPARISONS

<u>Comparison</u>	<u>Logrank</u>	<u>P-Value</u>
RH Officer vs RH Enlisted	-1.468	0.142
RH Flyers vs RH Ground	-1.455	0.146
Comparison Officer vs Comp Enlisted	-2.597	0.009
Comparison Flyers vs Comp Ground	-0.363	0.717

The SMR and logrank analyses are somewhat in agreement, with both procedures finding significant differences between comparison officers and comparison enlisted, with the officers living longer. The two methods approximately agree on the Ranch Hand fliers versus ground personnel and on Ranch Hand officer versus enlisted personnel with the logrank result near significance at the .10 level; the fliers appear to be living longer than the ground personnel within the Ranch Hand group.

4. Cause Specific Ranch Hand Versus Comparison Mortality

Cause specific mortality, relative risks, two-sided P-values for testing relative risk equal to unity, power and 95% confidence intervals for relative risks are summarized in Table 18 for the 1241 matched Ranch Handers and their mortality comparisons. Mortality data for the six unmatched Ranch Handers were not used in this analysis. Of the six, one has died of an accident and the rest are still alive. In some categories, the data were too sparse for relative risk estimation.

Table 18

CAUSE SPECIFIC MORTALITY AND RELATIVE RISKS

<u>Cause</u>	<u>Dead</u>		<u>Relative Risk</u>	<u>95% Conf Int.</u>	<u>P-value</u>	<u>Power</u>
	<u>RH</u>	<u>Comparison</u>				
Accidental	18	92	.959	(.466 - 1.453)	.875	.047
Suicide	3	14	1.071	(0 - 2.407)	.913	.061
Homicide	2	3	3.333	(0 - 9.297)	.099	.489
Infectious, Parasitic	0	3				
Malignant Neoplasm	4	39	.503	(0 - 1.024)	.205	.153
Uncertain Neoplasm	0	2				
Endocrine	1	1	5.000	(0 -18.859)	.102	.562
Mental Disorder	0	1				
Nervous System	0	2				
Circulatory	16	70	1.002	(.411 - 1.594)	.994	.050
Respiratory	0	4				
Digestive	5	11	2.273	(0 - 4.675)	.085	.457
Genitourinary	0	3				
Ill Defined	0	2				
Unknown	0	3				
	<u>49</u>	<u>250</u>				

The low powers in Table 18 reflect the sparseness of data or the fact that some of the observed relative risks approach unity. However, two categories do stand out as deserving further attention: malignant neoplasms and digestive system deaths. It should be noted that if matched sets are ignored and relative risk is estimated using the method of Mantel and Haenszel (14), these results remain essentially unchanged; using this approach, the relative risk for malignant neoplasms, for example, is .506 with a P-value of .195 and power equal to .254. The 95% confidence interval for relative risk using this approach is .180 to 1.419. The Mantel-Haenszel relative risk for the digestive system comparison is 2.254, with a P-value of .132 and a power equal to .325; the 95% confidence interval for relative risk is .782 to 6.501. The digestive system deaths are further defined in Table 19. There has been an increase in deaths due to liver disease among the Ranch Handers; however, this observed difference is not statistically significant. These data are also based on death certificate diagnoses and will be subjected to verification and validation from medical record and autopsy reports. When all deaths from liver disease are considered as a whole, a relative risk of 2.50 is found, with a 95% confidence interval of 0 to 5.501. The P value is 0.083. Similarly, the relative risk for pancreatitis is 2.50 with a 95% confidence interval of 0 to 8.501.; the P value is 0.386. These observations are of interest and will be pursued in depth in subsequent reports.

Table 19

DIGESTIVE SYSTEM MORTALITY

<u>ICD Code (9th Ed)</u>	<u>Deaths</u>	
	<u>Ranch Hand</u>	<u>Comparison</u>
Pancreatitis (5770)	1	2
Alcoholic cirrhosis (5712)	0	3
Nonalcoholic cirrhosis (5715)	3	3
Nonalcoholic fatty liver (5718)	0	1
Chronic liver disease (5728)	0	1
Alcoholic liver disease (5711)	1	0
Duodenal ulcer (5325)	0	1
	<u>5</u>	<u>11</u>

Table 20

SITE SPECIFIC MALIGNANT NEOPLASM MORTALITY

<u>Site ICD Code (9th Ed)</u>	<u>Deaths</u>	
	<u>Ranch Hand</u>	<u>Comparison</u>
Lip, oral cavity, Pharynx (140-149)	0	4
Digestive organs, peritoneum (150-159)	0	8
Respiratory, intrathoracic (160-165)	2	15
Bone, connective tissue, skin, breast (170-175)	0	1
Genitourinary organs (179-189)	1	3
Brain (191-192)	0	3
Lymphatic and hematopoietic tissue (200-208)	0	4
No site specification (199)	1	1
	<u>4</u>	<u>39</u>

The malignant neoplasms are detailed in Table 20, the cell types of the neoplasms, as recorded on the death certificates, are summarized in Table 21.

Table 21

MORPHOLOGY OF NEOPLASMS

ICD Code 9th Ed.	Nomenclature	Deaths	
		Ranch Hand	Comparison
M800	Neoplasms not otherwise specified (NOS)		
	Brain	0	1
	Bronchus and Lung	0	3
	Colon	0	1
	Intestinal Tract	0	1
M801-804	Epithelial neoplasms (NOS)		
	Bronchus and Lung	1	8
	Esophagus	0	1
	Kidney	1	1
	Nasopharynx	0	1
	Pancreas	0	2
	Unspecified site	1	1
M805-808	Papillary and Squamous Cell		
	Nasal Sinus	0	1
	Lip	0	1
	Tongue	0	1
	Tonsil	0	1
M814-838	Adenomas and Adenocarcinomas		
	Appendix	0	1
	Bronchus and Lung	0	2
	Colon	0	1
	Kidney	0	2
	Stomach	0	1
M872-879	Nevi and Melanomas		
	Skin (NOS)	0	1
	Mediastinal	1	0
M905	Mesothelioma		
	Bronchus and Lung	0	1
M938-948	Gliomas		
	Frontal Lobe	0	1
	Brain (NOS)	0	1
M959-963	Lymphomas NOS and Diffuse		
	Lymphomas (NOS)	0	1
M965-966	Hodgkins disease		
	Hodgkin's (NOS)	0	2
M986	Myeloid Leukemias		
	Acute Myelocytic Leukemia	0	1
		<u>4</u>	<u>39</u>

Epithelial, papillary and adenomas account for 64% of the comparison neoplasms. Three Ranch Hand neoplasms arose from epithelial cells. There were no tumors in either group which were classified as soft tissue sarcoma.