

Chapter VII

CONCLUSION

1. Introduction

The mortality analyses described in this report have not revealed any adverse death experience in the herbicide/dioxin exposed cohort. The results of the analyses, regardless of the source of the comparison data, were consistent: at this time, there is no indication that operation Ranch Hand personnel have experienced any increased mortality or any unusual patterns of death in time or by cause. They are not dying in increased numbers, at earlier ages, or by unexpected causes.

The fact that only a relatively small number of Ranch Hand deaths were available for analysis is reassuring in itself. However, the fact that adverse effects have not yet been detected does not imply that an effect will not become manifest at a future time or after covariate adjusted analyses. For this reason, further analyses are intended and mortality in the study population will be ascertained annually for the next 20 years.

A summary of the statistical techniques applied to each source of comparison data is presented in Table 42. It should be noted here that these analyses have been carried out without knowledge of covariate information, such as herbicide exposure, industrial chemical exposure, or other risk factors and that these analyses were carried out at a time when approximately 96% of Ranch Handers and their matched comparison subjects were still living. The data, therefore, must be viewed as preliminary to more definitive analyses, which will be performed over the next 20 years. Table 43 summarizes the results of the noncause specific analyses by source of the comparison data, and Table 44 presents the results of the cause specific analyses.

Table 42

SUMMARY OF STATISTICAL PROCEDURES USED IN ANALYSIS

Comparison Database	Internal Comparison Group	1978 U.S. White Males	1978 DoD Life Tables	West Point Class of 1956
<u>Noncause Specific Analyses</u>				
Logrank & Wilcoxon Procedures	+			+
Ejigou-McHugh Relative Risk	+			
Mantel-Haenszel Relative Risk	+			+
SMR/Breslow-Day Product Model	+			+
Gail-Ware Procedure		+	+	
<u>Cause Specific Analyses</u>				
Ejigou-McHugh Relative Risk	+			
Mantel-Haenszel Relative Risk	+			+

Procedure usage is indicated by a "+" symbol.

SUMMARY OF NONCAUSE SPECIFIC MORTALITY ANALYSES BY SOURCE
OF COMPARISON DATA

	Internal Comparison Group	1978 US White Males ¹	1978 DoD Life Tables ¹	West Point Class of 1956 ²
Ranch Hand Group	RH = C RH _O = C _O RH _E = C _E RH _F = C _F RH _G = C _G	RH <<<US RH _O <<<US RH _E ≤US	RH _O <<<DoD _O RH _E = DoD _E	RH _O = WP _O
Comparison Group		C <<<US C _O <<<US C _E <<<US	C _O < DoD _O C _E <<DoD _E	C _O = WP _O
Internal Occupational Group Specific	RH _O ≤ RH _E RH _F ≤ RH _G C _O < C _E C _F = C _G			

=	P value ³ greater than .10	RH Ranch Hand Group
≤	P value equal to or less than .10	C Comparison Group
<	P value equal to or less than .05	O Officers
<<	P value equal to or less than .01	E Enlisted
<<<	P value equal to or less than .001	F Flying
		G Ground

- 1 Validity of these comparisons is questionable (see Chapter 4)
- 2 Statistical inference is limited by small sample size
- 3 All P value symbols are based upon SMR and Gail-Ware analysis

Table 44

SUMMARY OF CAUSE SPECIFIC ANALYSES
BY SOURCE OF COMPARISON DATA

<u>RH Versus Internal Comparison</u>	<u>RH Versus West Point*</u>
No significant difference in cause specific relative risks	No significant difference in cause specific relative risks

* Statistical inference is limited by small sample size

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.