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The Air Force Health Study

An Epidemiologic Investigation of Health Effects in Air Force Personnel Following Exposure to Herbicides
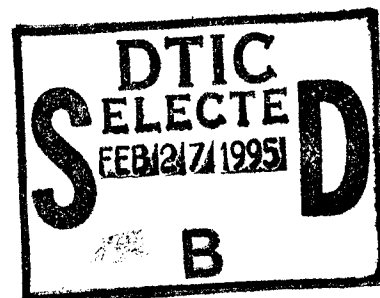
Mortality Update - 1993

William H. Wolf, Colonel, USAF, MC
Joel E. Michalek, Ph.D.
Judson C. Miner, Colonel, USAF, BSC

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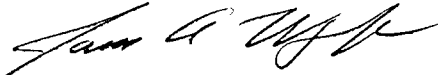FEB 27 1995
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The Office of Public Affairs has reviewed this technical report, and it is releasable to the National Technical Information Service, where it will be available to the general public, including foreign nationals.

This technical report has been reviewed and is approved for publication.

JOEL E. MICHALEK
Project Scientist

JAMES A. WRIGHT, Colonel, USAF, MC, CFS
Chief, Epidemiologic Research Division

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6. AUTHOR(S)
William H. Wolfe
Joel E. Michalek
Judson C. Miner

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES)
Armstrong Laboratory (AFMC)
Aerospace Medicine Directorate
Epidemiologic Research Division
2510 Kennedy Circle, Ste 117
Brooks Air Force Base, TX 78235-5119

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13. ABSTRACT (Maximum 200 words)

The purpose of the Air Force Health Study is to determine whether those individuals involved in the spraying of herbicides in Vietnam during the Ranch Hand operation have experienced any adverse health effects as a result of their participation in that program. The study is designed to evaluate both the mortality (death) and morbidity (disease) in these individuals over a 20-year period beginning in 1982.

The overall all-cause mortality experience of the Ranch Hands is not significantly different from the expected. As of 31 December 1991, 106 (8.4%) of the 1261 Ranch Hands have died; the expected number of deaths is 103. The observed and expected numbers of deaths were not significantly different for accidental deaths, suicides and deaths caused by malignant neoplasms and circulatory system diseases. However, there were significantly increased numbers of Ranch Hand deaths due to digestive diseases and, in nonflying enlisted personnel, circulatory system diseases. Both of these increases have been noted in previous reports and both are, as yet, unexplained.

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EXECUTIVE SUMMARY

An evaluation of cumulative all-cause Ranch Hand mortality through 31 December 1991 found no statistically significant differences between the observed and expected number of deaths (SMR=1.03, 95% CI 0.85-1.24, p=0.75). The indirectly standardized all-cause Ranch Hand death rate is 3.25 deaths per 1,000 person-years; the Comparison rate is 3.16 deaths per 1,000 person-years. Furthermore, the observed number of deaths is not statistically different from the expected number in any of the four subgroups of Ranch Hands determined by rank (officer, enlisted) and job (flyer, nonflyer).

There was a borderline significant increasing trend in the relative risk of death from any cause during the period 1989 through 1991 among flying Ranch Hand enlisted personnel. Of the seven deaths during that period, 5 were due to malignant neoplasm. Enlisted flyers were, as a group, less exposed to dioxin than enlisted nonflyers. Hence, while this trend is a source of concern, the lack of a corresponding trend among the more heavily exposed enlisted nonflyers suggests that this trend may not be caused by dioxin exposure.

Adjusted cause-specific analyses revealed no overall significant differences between the observed and expected numbers of deaths for accidental deaths (SMR=1.16), suicides (SMR=0.73), homicides (SMR=1.21), deaths due to infectious or parasitic diseases (SMR=1.89), deaths due to malignant neoplasm (SMR=0.85), endocrine disease (SMR=1.34) or deaths due to circulatory disease (SMR=1.10). However, there is a significant excess due to circulatory system diseases among nonflying enlisted personnel (SMR=1.57, 95% CI 1.01-2.33, p=0.05). The significant increase in deaths due to circulatory system deaths in nonflying enlisted personnel was noted in the last report. The number of these deaths has increased from 19 to 22 and the SMR has decreased slightly from 1.68 to 1.57 since the last report.

There is a significant excess of Ranch Hand deaths caused by diseases of the digestive system (SMR=2.23, 95% CI 1.09-4.10, p=0.03). This excess of Ranch Hand deaths was also noted in the last report and the number of such deaths has remained at nine since then. A significant excess of such deaths was found among Ranch Hand flying officers (SMR=3.33, 95% CI 1.06-8.03, p=0.04), although there were only four deaths in this stratum.

Analysis of survival status versus current dioxin levels found no significant difference between mean dioxin levels among living and dead Ranch Hands among the 872 Ranch Hands with dioxin results. Survival time was also not significantly associated with dioxin levels in Ranch Hands.

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In summary, the overall all-cause mortality experience of the Ranch Hands is not significantly different from that expected. As of 31 December 1991, 106 (8.4%) of the 1261 Ranch Hands have died; the expected number of deaths is 103. The observed and expected numbers of deaths were not significantly different for accidental deaths, suicides and deaths caused by malignant neoplasms and circulatory system diseases. However, there were significantly increased numbers of Ranch Hand deaths due to digestive diseases and, in nonflying enlisted personnel, circulatory system diseases. Both of these increases have been noted in previous reports and both are, as yet, unexplained.

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1. INTRODUCTION

This report updates the findings of prior Air Force Health Study mortality reports released in 1983 [1], 1984 [2], 1985 [3], 1986 [4], 1989 [5] and 1991 [6]. The reader is referred to the baseline report [1] for information regarding the study design and the mortality determination process.

This report contrasts cumulative Ranch Hand mortality through 31 December 1991 (verified as of 15 March 1993) with that expected based on the mortality experience of the Comparison population of 19,080 Air Force veterans who flew or serviced C-130 cargo aircraft in Southeast Asia (SEA) during the same calendar period that the Ranch Hand unit was active in Vietnam.

Table 1 shows summary counts, person-years and death rates by group (Ranch Hand, Comparison). A person-year is the length of time lived by one person in one year. Persons surviving to the time of data analysis contribute the time, in years, between the dates of entry into follow-up and the date of data analysis. Persons known to have died before the date of data analysis contribute the time, in years, between the dates of entry into follow-up and death. In this study, the date of entry into follow-up is the date of start of duty in SEA. The date of data analysis is 31 December 1991. All analyses are based on regression analysis of the Standardized Mortality Ratio (SMR), the ratio of the observed to the expected number of deaths [7]. P-values and confidence intervals for the SMR were computed based on a Poisson model [8]. Except when otherwise noted, all death rates (per 1,000 person years), expected deaths and SMR's are adjusted for year of birth, age, rank (officer, enlisted) and military occupation (flyer, nonflyer).

In the hypothetical case that the Ranch Hand mortality experience is the same as that of the Comparisons, about 5% of the many statistical analyses shown in this report should be expected to produce p-values less than 0.05. The observation of significant results due to multiple testing on the same data, even when there is no group difference, is known as the multiple testing artifact and is common to all large studies. Hence, each significant result is assessed for consistency with known exposure differences between subgroups of Ranch Hands based on rank and occupation. Nonflying enlisted personnel have higher current dioxin levels than officers and flying enlisted personnel have intermediate levels [9].

2. ALL CAUSE MORTALITY

Summary mortality statistics for both populations are given in Table 1. In Table 1 and throughout this report, "flying officers" refers to pilots and navigators. "Officers" are flying officers and nonflying officers. "Flying enlisted personnel" are enlisted flight engineers. "Nonflying enlisted personnel" are enlisted ground personnel. All Ranch Hand death rates in Table 1 are adjusted via indirect standardization. Each indirectly standardized rate is the product of the Comparison death rate and the adjusted SMR (Table 3). The result is then multiplied by 1,000 to give a death rate per 1,000 person-years.

Table 1

Summary Counts and Adjusted Death Rates
by Rank and Occupation, All Causes

	Ranch Hand				Comparison			
Stratum	At Risk	Dead	Person Years	Rate	At Risk	Dead	Person Years	Rate
Flying Officers	441	35	10368	3.39	5242	430	124524	3.45
Flying Enlisted	207	19	4886	3.22	2829	262	66227	3.96
All Flyers	648	54	15254	3.32	8071	692	190751	3.63
Nonflying Officers	26	2	610	3.40	284	21	6919	3.04
Nonflying Enlisted	587	50	13777	3.33	10725	726	258190	2.81
All Nonflyers	613	52	14387	3.33	11009	747	265109	2.82
All Officers	467	37	10978	3.39	5526	451	131443	3.43

Table 1 (continued)

	Ranch Hand				Comparison			
Stratum	At Risk	Dead	Person Years	Rate	At Risk	Dead	Person Years	Rate
All Enlisted	794	69	18663	3.21	13554	988	324417	3.05
All Personnel	1261	106	29640	3.25	19080	1439	455860	3.16

Unadjusted occupation and race-specific mortality is summarized in Table 2.   Some Ranch Hand death rates in Table 2 appear unusually high.   For example, the Ranch Hand death rate among Black enlisted flight engineers is 11.70 deaths per 1,000 person-years and the corresponding rate for all Comparison deaths in this stratum is 5.23 deaths per 1,000 person-years.   The four Ranch Hand deaths in this stratum have occurred since 1980.   One of the four deaths was a suicide, one was accidental, one was due to a digestive system disease and one was due to ill-defined causes.   An adjusted analysis shows that this increase is not statistically significant (SMR=2.0, 95% CI 0.64-4.83, p=0.20). In general, a death rate based on only a few deaths is not a reliable measure of mortality experience because one additional death can produce large changes in the death rate and the SMR.

Table 2

Unadjusted Occupation and Race Specific Cumulative All-cause Mortality

a) Nonblack Personnel

| Stratum | Ranch Hand | | | | Comparison | | | |
	At Risk	Dead	Person Years	Rate	At Risk	Dead	Person Years	Rate
Pilots	351	27	8236	3.28	3417	306	80886	3.78
Navigators	82	8	1947	4.11	1773	123	42344	2.90
Nonflying Officers	25	2	587	3.41	280	21	6823	3.08
Flying Enlisted	192	15	4544	3.30	2606	235	61061	3.85
Nonflying Enlisted	534	45	12534	3.59	9689	636	233612	2.72
Total	1184	97	27849	3.48	17765	1321	424726	3.11

b) Black Personnel

| Stratum | Ranch Hand | | | | Comparison | | | |
	At Risk	Dead	Person Years	Rate	At Risk	Dead	Person Years	Rate
Pilots	6	0	139	0.00	20	1	490	2.04
Navigators	2	0	46	0.00	32	0	804	0.00
Nonflying Officers	1	0	23	0.00	4	0	96	0.00
Flying Enlisted	15	4	342	11.70	223	27	5166	5.23

Table 2 (continued)

Stratum	Ranch Hand				Comparison			
	At Risk	Dead	Person Years	Rate	At Risk	Dead	Person Years	Rate
Nonflying Enlisted	53	5	1243	4.02	1036	90	24577	3.66
Total	77	9	1791	5.03	1315	118	31134	3.79

c) All Personnel

Stratum	Ranch Hand				Comparison			
	At Risk	Dead	Person Years	Rate	At Risk	Dead	Person Years	Rate
Pilots	357	27	8375	3.22	3437	307	81376	3.77
Navigators	84	8	1993	4.01	1805	123	43148	2.85
Nonflying Officers	26	2	610	3.28	284	21	6919	3.04
Flying Enlisted	207	19	4886	3.89	2829	262	66227	3.96
Nonflying Enlisted	587	50	13777	3.63	10725	726	258190	2.81
Total	1261	106	29640	3.58	19080	1439	455860	3.16

Survival analyses were carried out to assess Ranch Hand all-cause mortality relative to the Comparison population. All analyses were adjusted for rank (officer, enlisted), occupation (flyer, nonflyer) and date of birth and age in 5-year intervals. The results are shown in Table 3. The expected numbers of deaths in Table 3 are sums of expected numbers of deaths within 5-year intervals of year of birth.

Table 3

Adjusted All-cause Standardized Mortality Ratios
by Rank and Military Occupation Among Ranch Hands

Stratum	Dead	Expected Deaths	SMR	95% C.I.	P-value
Flying Officers	35	35.67	0.98	0.70-1.35	0.95
Nonflying Officers	2	1.78	1.12	0.19-3.70	0.80
All Officers	37	37.45	0.99	0.71-1.35	0.98
Flying Enlisted	19	23.34	0.81	0.50-1.25	0.37
Nonflying Enlisted	50	42.21	1.18	0.89-1.55	0.24
All Enlisted	69	65.55	1.05	0.83-1.32	0.66
All Flying Personnel	54	59.01	0.92	0.70-1.19	0.53
All Nonflying Personnel	52	43.99	1.18	0.89-1.54	0.23
All Ranch Hands	106	103.00	1.03	0.85-1.24	0.75

There are no significant differences between the observed and expected number of deaths from all causes in any stratum. The overall adjusted SMR for all Ranch Hands for all causes of death is 1.03, 95% CI, 0.85-1.24, p=0.75.

Chi-square tests for trend were applied to all strata to assess the significance of trends in the SMR since 1985. These analyses were carried out twice, first with each of the years 1985 through 1991 separately contributing to the test statistic and again with 1985 through 1988 collapsed to a single stratum and 1989 through 1991 collapsed to a second stratum. All analyses are conditioned on survival to 1 January 1985 and due to sparseness were not adjusted for date of birth. These tests are two-tailed and therefore would detect upward or downward trends in the SMR. Test results for detecting upward trends in the SMR may be derived from these results by dividing the p-value by two when the data indicate an increasing trend and replacing the p-value by 1.00 when the data indicate a decreasing trend. The results are shown in Table 4.

Table 4

All-cause Ranch Hand Mortality
Seven-year Trend Analysis

Flying Officers

Chi-square(single year) =3.18   P =0.07
Chi-square(85-88,89-91) =4.13   P =0.04

Year	Dead	Rate	Expected Deaths	SMR
1985	1	2.35	1.45	0.69
1986	5	11.84	1.79	2.80
1987	5	11.94	2.55	1.96
1988	5	12.11	2.69	1.86
1989	2	4.88	1.76	1.13
1990	2	4.91	2.44	0.82
1991	0	0.00	2.02	0.00

Enlisted Flyers

Chi-square(single year) =2.23   P =0.14
Chi-square(85-88,89-91) =3.58   P =0.06

Year	Dead	Rate	Expected Deaths	SMR
1985	1	5.07	0.89	1.12
1986	1	5.08	1.26	0.79
1987	1	5.11	0.89	1.12
1988	0	0.00	1.42	0.00
1989	1	5.13	0.82	1.21
1990	3	15.56	0.97	3.10
1991	3	15.78	1.25	2.39

Table 4 (continued)

All Flyers

Chi-square(single year) $=0.27$ $P =0.60$
Chi-square(85-88,89-91) $=0.32$ $P =0.57$

Year	Dead	Rate	Expected Deaths	SMR
1985	2	3.21	2.36	0.85
1986	6	9.70	3.09	1.94
1987	6	9.77	3.41	1.76
1988	5	8.22	4.12	1.21
1989	3	4.96	2.59	1.16
1990	5	8.33	3.39	1.48
1991	3	5.03	3.30	0.91

Nonflying Officers

Chi-square(single year) $=1.61$ $P =0.20$
Chi-square(85-88,89-91) $=5.35$ $P =0.02$

Year	Dead	Rate	Expected Deaths	SMR
1985	0	0.00	0.09	0.00
1986	0	0.00	0.18	0.00
1987	0	0.00	0.37	0.00
1988	0	0.00	0.37	0.00
1989	1	40.54	0.09	10.73
1990	0	0.00	0.09	0.00
1991	0	0.00	0.00	0.00

Table 4 (continued)

Nonflying Enlisted Personnel

Chi-square(single year) =0.22   P =0.64
Chi-square(85-88,89-91) =1.37   P =0.24

Year	Dead	Rate	Expected Deaths	SMR
1985	2	3.59	2.16	0.93
1986	3	5.42	1.89	1.59
1987	2	3.63	2.37	0.84
1988	6	10.96	2.69	2.23
1989	1	1.84	2.58	0.39
1990	4	7.38	3.01	1.33
1991	2	3.71	2.85	0.70

All Nonflyers

Chi-square(single year) =0.09   P =0.76
Chi-square(85-88,89-91) =0.64   P =0.42

Year	Dead	Rate	Expected Deaths	SMR
1985	2	3.44	2.26	0.89
1986	3	5.19	2.03	1.48
1987	2	3.47	2.63	0.76
1988	6	10.48	2.96	2.03
1989	2	3.52	2.68	0.75
1990	4	7.07	3.12	1.28
1991	2	3.56	2.90	0.69

Table 4 (continued)

All Officers

Chi-square(single year) =2.35   P =0.13
Chi-square(85-88,89-91) =2.45   P =0.12

Year	Dead	Rate	Expected Deaths	SMR
1985	1	2.22	1.54	0.65
1986	5	11.18	1.97	2.54
1987	5	11.27	2.90	1.73
1988	5	11.42	3.05	1.64
1989	3	6.91	1.86	1.61
1990	2	4.64	2.53	0.79
1991	0	0.00	2.03	0.00

All Enlisted Personnel

Chi-square(single year) =0.19   P =0.66
Chi-square(85-88,89-91) =0.00   P =0.97

Year	Dead	Rate	Expected Deaths	SMR
1985	3	3.98	3.02	0.99
1986	4	5.33	3.02	1.32
1987	3	4.02	3.25	0.92
1988	6	8.08	4.00	1.50
1989	2	2.71	3.42	0.58
1990	7	9.52	4.00	1.75
1991	5	6.86	4.05	1.24

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Table 4 (continued)

All Ranch Hands

Chi-square(single year) =0.41   P =0.52
Chi-square(85-88,89-91) =1.10   P =0.30

Year	Dead	Rate	Expected Deaths	SMR
1985	4	3.32	4.63	0.86
1986	9	7.52	4.95	1.82
1987	8	·6.72	5.93	1.35
1988	11	9.32	6.89	1.60
1989	5	4.26	5.32	0.94
1990	9	7.72	6.49	1.39
1991	5	4.32	6.15	0.81

There is a significant downward trend among flying officers
(p=0.04) caused by relatively low death rates after 1988. A
borderline significant upward trend among flying enlisted
personnel (p=0.06) is caused by increased death rates after 1988.

Of the seven flying enlisted ground personnel who died after
1988, one died in 1989 of suicide, three died in 1990 of
malignant neoplasm, two died in 1991 of malignant neoplasm and
one died in 1991 of coronary atherosclerosis. Of the five deaths
due to malignant neoplasm, one was specified as "other,
unspecified site, adenocarcinoma NOS", one was "other,
unspecified site, squamous cell carcinoma NOS", one was "liver
not specified, carcinoma NOS", one was "colon, unspecified,
carcinoma NOS" and one was "multiple myeloma, plasma cell
myeloma".

A lexis diagram [10] for Ranch Hand flying officers is shown in
Figure 1. Follow-up time is indicated for each living subject
with a straight line beginning at his age at the beginning of his
first qualifying tour of duty in SEA and ending with his age at
31 December 1991. Follow-up lines for deceased subjects end with
a square at the subject's age at death and date of death. The
corresponding diagram without the follow-up lines is shown in
Figure 2. Lexis diagrams for nonflying officers, flying enlisted
and nonflying enlisted personnel, without follow-up lines, are
shown in Figures 3 through 5.

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Lexis diagrams provide another view of the data that permits a visual assessment of mortality clustering with respect to age and calendar time. A strong latency effect, for example, might be revealed by a cluster of deaths approximately 20 years after entry into follow-up. No such clusters are apparent in these data.

Figure 1
Lexis Diagram
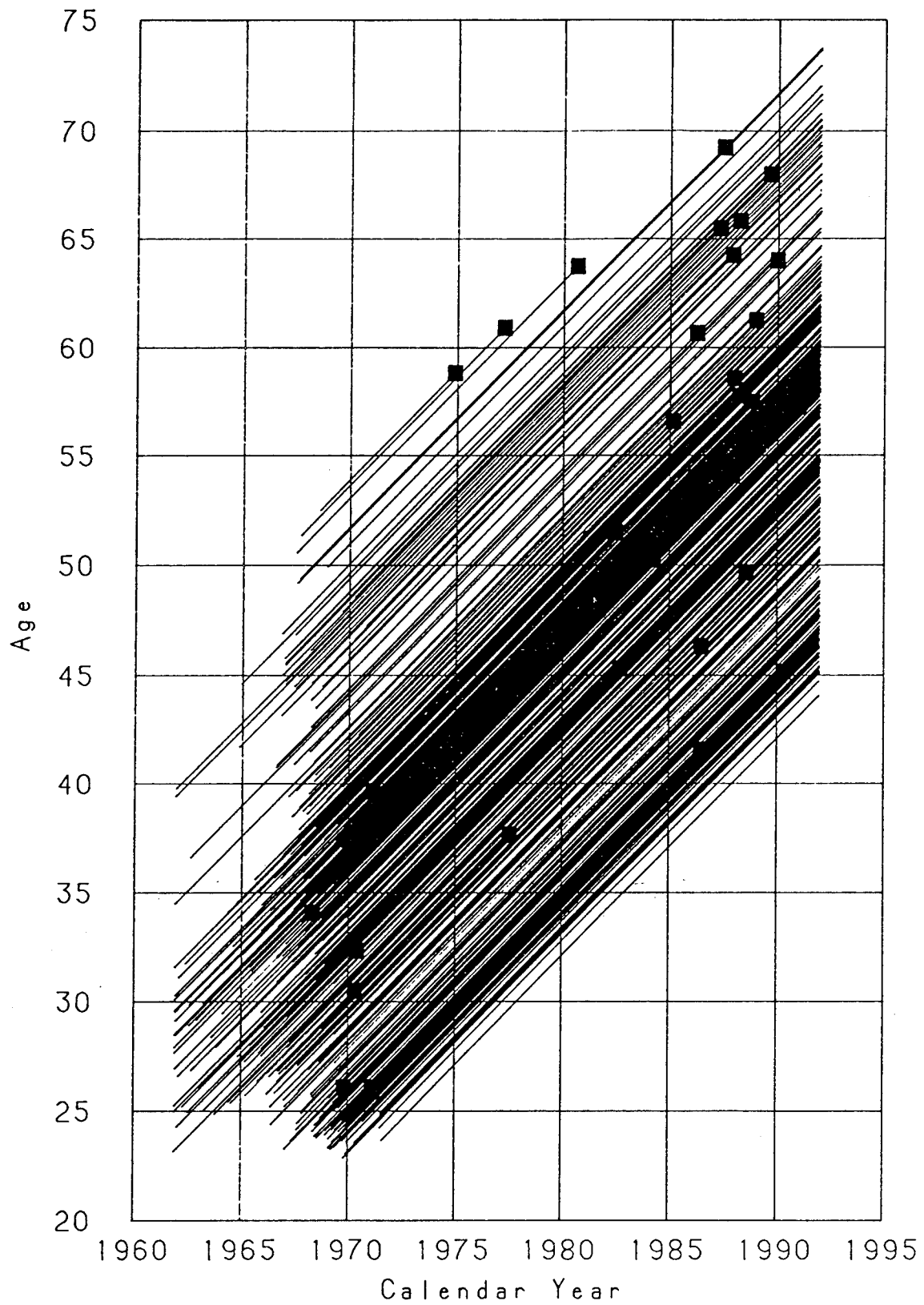Ranch Hand Flying Officers

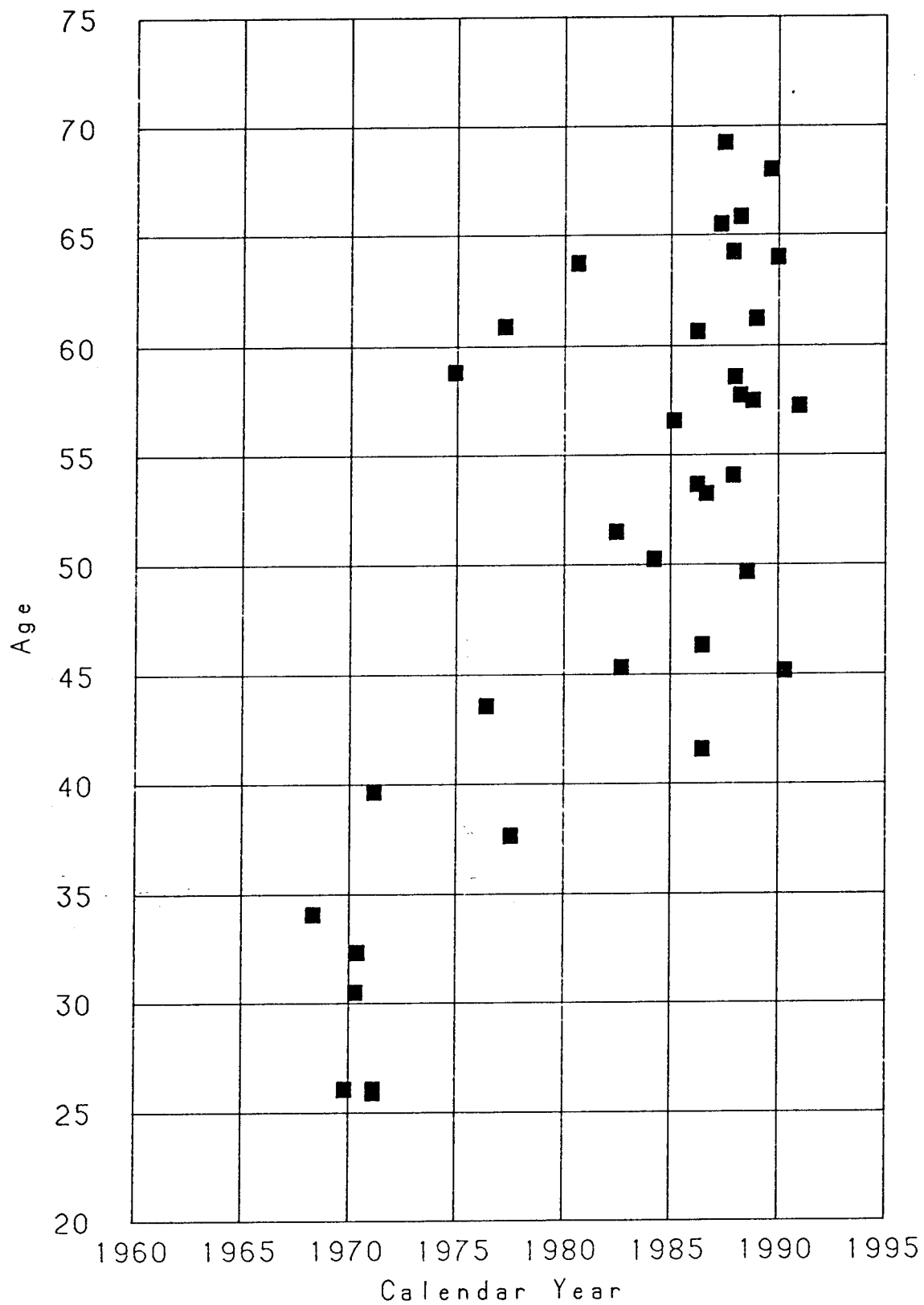Figure 2
Lexis Diagram
Ranch Hand Flying Officers

Figure 3
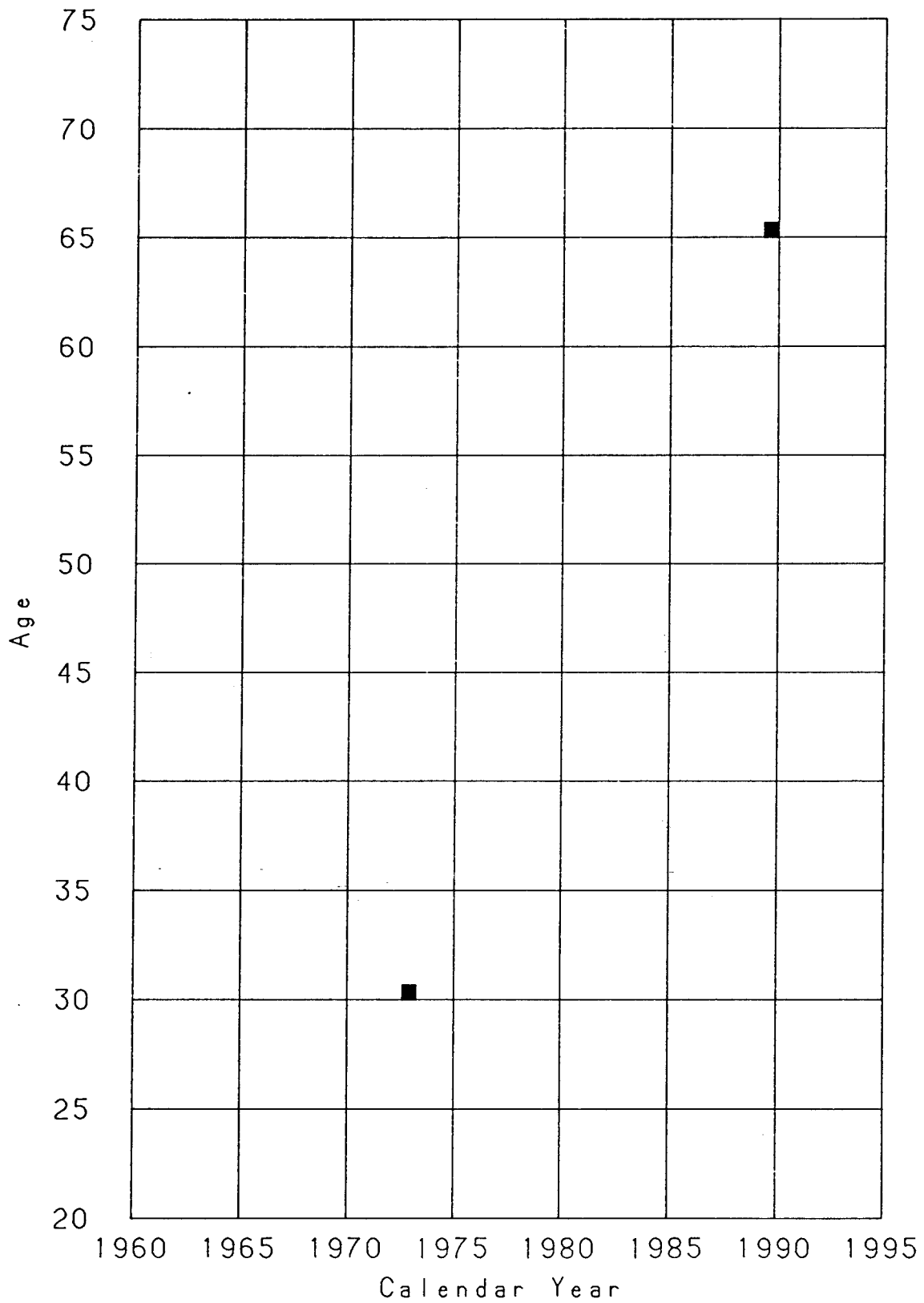Lexis Diagram
Ranch Hand Nonflying Officers

Figure 4
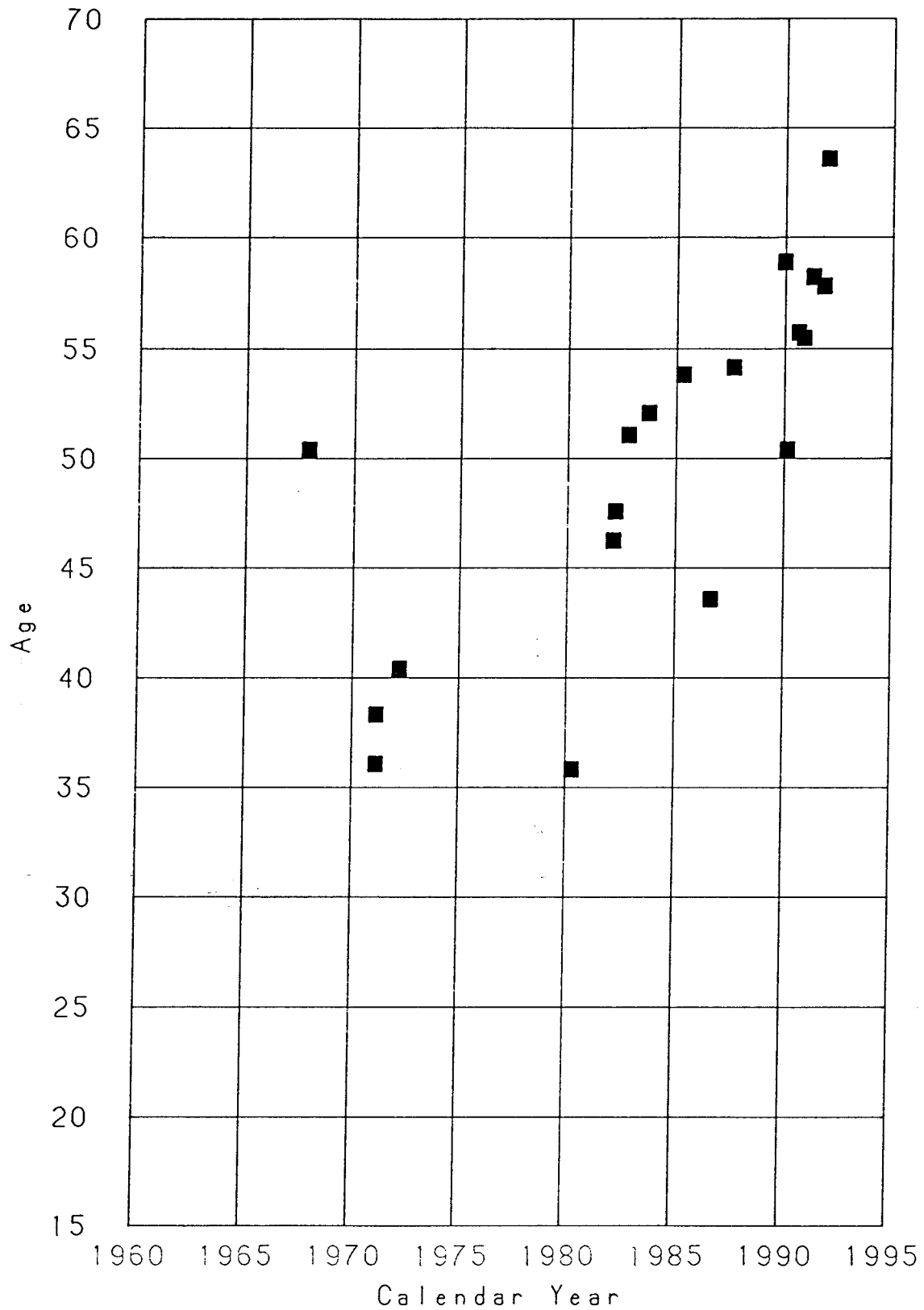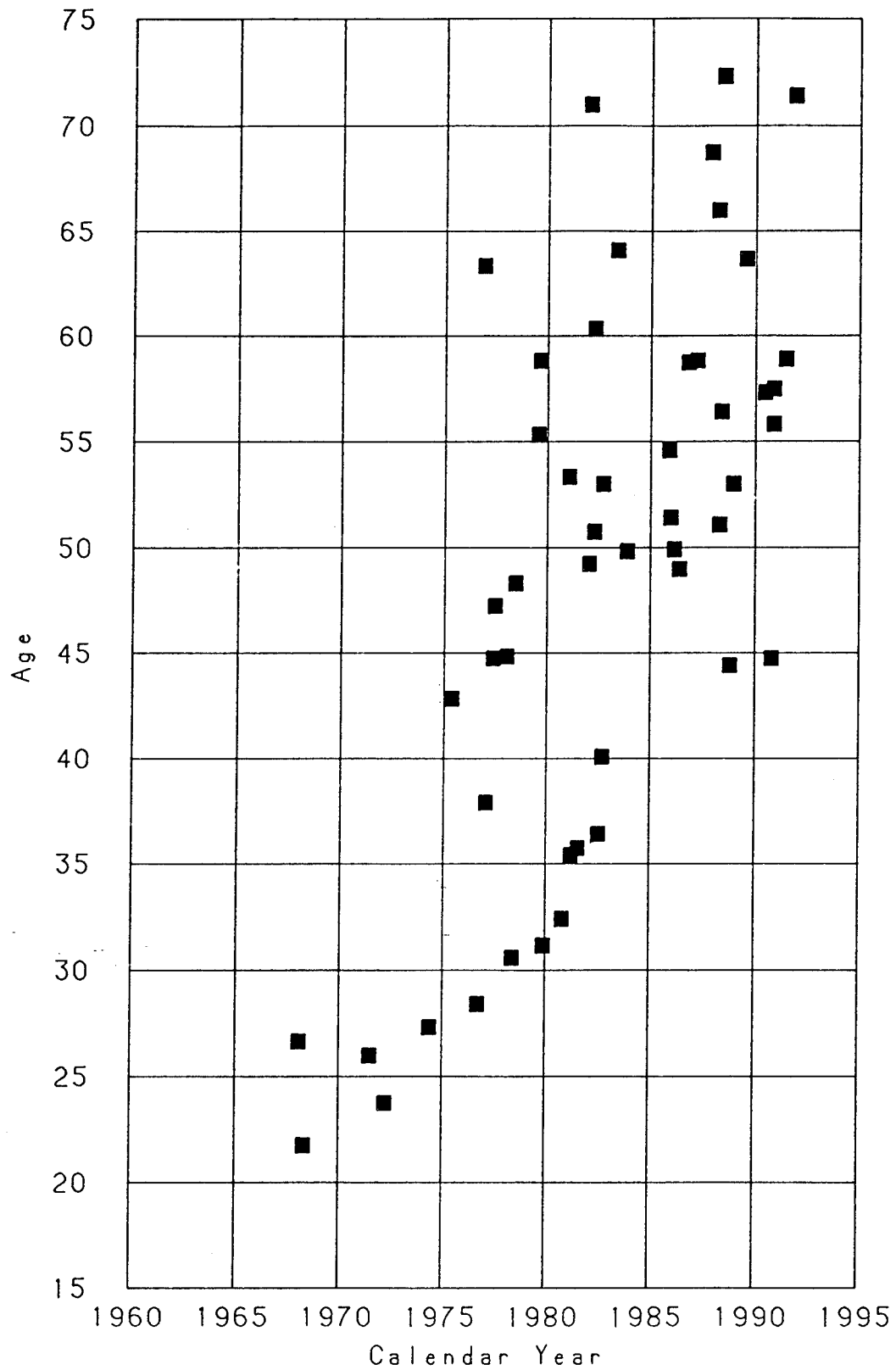Lexis Diagram
Ranch Hand Flying Enlisted

Figure 5
Lexis Diagram
Ranch Hand Nonflying Enlisted

3. CAUSE-SPECIFIC MORTALITY

Observed and adjusted expected Ranch Hand deaths by specific cause and stratum of rank and occupation are summarized in Table 5.

Table 5

Adjusted Cause-specific Ranch Hand Mortality by Rank and Occupation

Cause	Stratum	Dead	Expected Deaths	SMR	95% C.I.	P-value
Accident	Flying Officer	10	8.15	1.23	0.62-2.19	0.50
	Flying Enlisted	4	5.32	0.75	0.24-1.81	0.61
	Nonflying Officer	0	0.10	0.00		
	Nonflying Enlisted	11	8.07	1.36	0.72-2.37	0.31
	All Ranch Hands	25	21.64	1.16	0.76-1.68	0.46
Suicide	Flying Officer	0	1.44	0.00		
	Flying Enlisted	2	1.46	1.37	0.23-4.53	0.61
	Nonflying Officer	1	0.12	8.64	0.43-42.60	0.12
	Nonflying Enlisted	1	2.44	0.41	0.01-2.02	0.39
	All Ranch Hands	4	5.45	0.73	0.23-1.77	0.57
Homicide	Flying Officer	0	0.28	0.00		
	Flying Enlisted	0	0.42	0.00		
	Nonflying Officer	0	0.00			
	Nonflying Enlisted	2	0.95	2.10	0.35-6.94	0.32
	All Ranch Hands	2	1.65	1.21	0.20-3.99	0.72
Infectious-Parasitic	Flying Officer	1	0.53	1.88	0.09-9.28	0.51
	Flying Enlisted	0	0.10	0.00		
	Nonflying Officer	0	0.00			
	Nonflying Enlisted	1	0.43	2.34	0.12-11.55	0.42
	All Ranch Hands	2	1.06	1.89	0.32-6.24	0.38
Malignant Neoplasm	Flying Officer	7	9.81	0.71	0.31-1.41	0.38
	Flying Enlisted	6	6.22	0.96	0.39-2.01	0.98
	Nonflying Officer	1	0.58	1.73	0.09-8.51	0.56
	Nonflying Enlisted	9	10.52	0.86	0.42-1.57	0.67
	All Ranch Hands	23	27.13	0.85	0.55-1.25	0.44

Table 5 (continued)

Cause	Stratum	Dead	Expected Deaths	SMR	95% C.I.	p-value
Endocrine Disease	Flying Officer	0	0.18	0.00		
	Flying Enlisted	0	0.10	0.00		
	Nonflying Officer	0	0.00			
	Nonflying Enlisted	1	0.47	2.15	0.11-10.61	0.45
	All Ranch Hands	1	0.75	1.34	0.07-6.59	0.70
Circulatory Disease	Flying Officer	12	11.71	1.02	0.56-1.74	0.90
	Flying Enlisted	3	7.06	0.42	0.11-1.16	0.11
	Nonflying Officer	0	0.78	0.00		
	Nonflying Enlisted	22	14.06	1.57	1.01-2.33	0.05
	All Ranch Hands	37	33.61	1.10	0.79-1.50	0.55
Digestive Disease	Flying Officer	4	1.20	3.33	1.06-8.03	0.04
	Flying Enlisted	2	1.33	1.51	0.25-4.98	0.53
	Nonflying Officer	0	0.10	0.00		
	Nonflying Enlisted	3	1.40	2.15	0.55-5.84	0.22
	All Ranch Hands	9	4.03	2.23	1.09-4.10	0.03
Ill-Defined Unknown	Flying Officer	1	0.25	3.95	0.20-19.50	0.25
	Flying Enlisted	2	0.33	6.11	1.02-20.17	0.05
	Nonflying Officer	0	0.00			
	Nonflying Enlisted	0	0.71	0.00		
	All Ranch Hands	3	1.29	2.32	0.59-6.32	0.18

There are no overall or within-stratum significant differences between observed and expected numbers of deaths due to accidents, suicides, homicides, infectious or parasitic diseases, malignant neoplasms or endocrine diseases (Table 5). There is a significantly increased number of deaths caused by diseases of the circulatory system among Ranch Hand nonflying enlisted personnel (SMR=1.57, 95% CI 1.01-2.33, p=0.05) and a significantly increased number of deaths due to digestive diseases in all Ranch Hands (SMR=2.23, 95% CI 1.09-4.10, p=0.03), with a significant excess among Ranch Hand flying officers (SMR=3.33, 95% CI 1.06-8.03, p=0.04). There was no significant increase in Ranch Hand deaths due to ill-defined or unkown causes, but the number of such deaths was significantly elevated among Ranch Hand flying enlisted personnel (SMR=6.11, 95% CI 1.02-20.17, p=0.05), although the number of deaths in this stratum is small (the observed number is 2 and the expected number is 0.33).

Table 6 shows cumulative site-specific malignant neoplasm mortality among Ranch Hands.

Table 6

Site-specific Malignant Neoplasm Ranch Hand Mortality

ICD Code	Site	Dead	Expected Deaths
140-149	Lip,Oral Cavity and Pharynx		
140.9	Lip, Unspecified	0	0.092
141.9	Tongue, Unspecified	0	0.193
144.9	Floor of Mouth, Unspecified	0	0.185
145.3	Soft Palate	0	0.092
145.9	Mouth, Unspecified	0	0.156
146.0	Tonsil	0	0.097
147.9	Nasopharynx, Unspecified	0	0.092
148.1	Pyriform Sinus	0	0.157
149.0	Pharynx, Unspecified	0	0.184
150-159	Digestive Organs and Peritoneum		
150.3	Oesophagus, Upper Third	0	0.052
150.5	Oesophagus, Lower Third	0	0.064
150.9	Oesophagus, Unspecified	1	0.903
151.9	Stomach, Unspecified	1	0.352
153.4	Colon, Caecum	0	0.090
153.5	Colon, Appendix	0	0.088
153.6	Ascending Colon	0	0.052
153.9	Colon, Unspecified	1	2.198
154.0	Rectosigmoid Junction	0	0.369
154.1	Rectum	0	0.300
154.3	Anus, Unspecified	0	0.092
155.0	Liver, Primary	0	0.000
155.1	Intrahepatic Bile Ducts	0	0.093
155.2	Liver, Unspecified	1	0.000
156.0	Gall Bladder	0	0.093
157.4	Islets of Langerhans	0	0.180
157.9	Pancreas, Unspecified	1	0.992
159.0	Intestinal Tract, Unspecified	0	0.092
160-165	Respiratory and Intrathoracic Organs		
160.9	Accessory Sinus, Unspecified	0	0.052
161.1	Supraglottis	0	0.087
161.9	Larynx, Unspecified	0	0.309
162.2	Main Bronchus	0	0.064
162.3	Upper Lobe, Bronchus or Lung	0	0.151
162.4	Middle Lobe, Bronchus or Lung	0	0.065

Table 6 (continued)

ICD Code	Site	Dead	Expected Deaths
162.9	Bronchus and Lung, Unspecified	10	10.500
163.9	Pleura, Unspecified	0	0.064
164.9	Mediastinum, Unspecified	1	0.052
170-175	Bone,Connective Tissue, Skin and Breast		
170.9	Bone and Articular Cartilage, Unsp	0	0.058
171.0	Head, Face and Neck	0	0.052
171.3	Lower Limb, Including Hip	1	0.000
171.5	Abdomen	0	0.090
171.8	Connective, Soft Tissue, Other	0	0.087
171.9	Site Unspecified	0	0.278
172.5	Skin, Trunk	0	0.065
172.9	Skin, Unspecified	0	0.615
179-189	Genitourinary Organs		
185.0	Prostate	0	0.433
188.9	Bladder, Unspecified	0	0.260
189.0	Kidney, Except Pelvis	1	0.506
190-199	Other and Unspecified Sites		
191.1	Brain, Frontal Lobe	0	0.052
191.4	Occipital Lobe	0	0.092
191.7	Brain Stem	0	0.116
191.9	Brain, Unspecified	1	0.804
195.0	Head, Face and Neck	0	0.519
195.8	Other Unspecified Site	0	0.064
199.1	Other, Unspecified	3	2.272
200-208	Lymphatic and Haematopoietic Tissue		
200.0	Reticulosarcoma	0	0.090
200.1	Lymphosarcoma	0	0.088
200.8	Reticulolymphosarcoma	0	0.092
201.9	Hodgkin's Disease, Unspecified	0	0.140
202.8	Other Lymphomas	0	0.452
203.0	Multiple Myeloma	1	0.877
204.0	Acute Lymphoid Leukaemia	0	0.056
204.1	Chronic Lymphoid Leukaemia	0	0.212
204.9	Lymphoid Leukaemia, Unspecified	0	0.123
205.0	Acute Myeloid Leukaemia	0	0.265
205.1	Chronic Myeloid Leukaemia	0	0.123
205.3	Myeloid Sarcoma	0	0.087
206.0	Acute Monocytoid Leukaemia	0	0.063
207.8	Lymphosarcoma Cell Leukaemia	0	0.087
208.0	Acute Leukaemia, Unspecified	0	0.157
	Totals	23	27.967

The 23 Ranch Hand deaths due to malignant neoplasm do not appear to aggregate in an unusual pattern relative to that expected (Table 6).

The morphology of cumulative malignant neoplasm deaths is summarized in Table 7.

Table 7

Morphology of Ranch Hand Malignant Neoplasms

Code	Morphology	Dead	Expected Deaths
M800	Neoplasms NOS		
140-149	Lip,Oral Cavity and Pharynx	0	0.065
150-159	Digestive Organs and Peritoneum	1	2.375
160-165	Respiratory and Intrathoracic Organs	4	4.285
179-189	Genitourinary Organs	0	0.570
190-199	Other and Unspecified Sites	1	1.225
M801-M804	Epithelial Neoplasms NOS		
140-149	Lip,Oral Cavity and Pharynx	0	0.373
150-159	Digestive Organs and Peritoneum	3	1.608
160-165	Respiratory and Intrathoracic Organs	6	4.706
170-175	Bone,Connective Tissue, Skin, Breast	0	0.090
179-189	Genitourinary Organs	1	0.251
190-199	Other and Unspecified Sites	1	0.695
M805-M808	Papillary and Squamous Cell Neoplasms		
140-149	Lip,Oral Cavity and Pharynx	0	0.717
150-159	Digestive Organs and Peritoneum	0	0.303
160-165	Respiratory and Intrathoracic Organs	0	0.687
190-199	Other and Unspecified Sites	1	0.469
M814-M838	Adenomas and Adenocarcinomas		
150-159	Digestive Organs and Peritoneum	1	1.814
160-165	Respiratory and Intrathoracic Organs	0	1.407
179-189	Genitourinary Organs	0	0.379
190-199	Other and Unspecified Sites	1	0.470
M856-M858	Complex Epithelial Neoplasms		
190-199	Other and Unspecified Sites	0	0.092
M872-M879	Naevi and Melanomas		
160-165	Respiratory and Intrathoracic Organs	1	0.000
170-175	Bone,Connective Tissue, Skin, Breast	0	0.679
M880	Soft Tissue Tumors & Sarcomas NOS		
170-175	Bone,Connective Tissue, Skin, Breast	0	0.273
190-199	Other and Unspecified Sites	0	0.065
M881-M883	Fibromatous Neoplasms		
140-149	Lip,Oral Cavity and Pharynx	0	0.093
170-175	Bone,Connective Tissue, Skin, Breast	1	0.000

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Table 7 (continued)

Code	Morphology	Dead	Expected Deaths
M885-M888 Lipotamous Neoplasms			
170-175 Bone,Connective Tissue, Skin, Breast		0	0.058
M905 Mesothelial Neoplasms			
160-165 Respiratory and Intrathoracic Organs		0	0.156
M906-M909 Germ Cell Neoplasms			
160-165 Respiratory and Intrathoracic Organs		0	0.052
190-199 Other and Unspecified Sites		0	0.058
M926 Miscellaneous Bone Tumours			
170-175 Bone,Connective Tissue, Skin, Breast		0	0.058
M938-M948 Gliomas			
190-199 Other and Unspecified Sites		0	0.845
M949-M952 Neuroepitheliomatous Neoplasms			
170-175 Bone,Connective Tissue, Skin, Breast		0	0.087
M959-M963 Lymphomas NOS or Diffuse			
200-208 Lymphatic and Haematopoietic Tissue		0	0.543
M964 Reticulosarcomas			
200-208 Lymphatic and Haematopoietic Tissue		0	0.177
M965-M966 Hodgkin's Disease			
200-208 Lymphatic and Haematopoietic Tissue		0	0.140
M973 Plasma Cell Tumours			
200-208 Lymphatic and Haematopoietic Tissue		1	0.877
M980 Leukaemia NOS			
200-208 Lymphatic and Haematopoietic Tissue		0	0.157
M982 Lymphoid Leukaemias			
200-208 Lymphatic and Haematopoietic Tissue		0	0.391
M985 Lymphosarcoma Cell Leukaemias			
200-208 Lymphatic and Haematopoietic Tissue		0	0.087
M986 Myeloid Leukaemias			
200-208 Lymphatic and Haematopoietic Tissue		0	0.389
M989 Monocytic Leukaemias			
200-208 Lymphatic and Haematopoietic Tissue		0	0.063
M990 Miscellaneous Leukaemias			
160-165 Respiratory and Intrathoracic Organs		0	0.052
200-208 Lymphatic and Haematopoietic Tissue		0	0.087
	Totals	23	27.967

Although the adjusted SMR for deaths due to malignant neoplasm is less than 1.0 (Table 5), there are morphologic subcategories of malignancies for which the SMR is greater than 1.0. For example, there are 11 Ranch Hand deaths from epithelial neoplasms not otherwise specified and the expected number of deaths in this category is 7.72. However, this excess is not signficant (SMR=1.42, 95% CI 0.75-2.48, p=0.27).

Table 8 shows the morphology, age at death and smoking history, in pack-years, of the 10 Ranch Hands who died of lung cancer (Table 6). One pack-year is defined as smoking one pack of cigarettes per day for one year.

Table 8

Morphology and Smoking Histories of 10 Ranch Hand
Lung Cancer Deaths

Sequence Number	Morphology	Age at death	Packyears
1	Neoplasm, NOS	59	6
2	Epithelial Neoplasm, NOS	68	97
3	Neoplasm, NOS	68	47
4	Epithelial Neoplasm, NOS	56	39
5	Epithelial Neoplasm, NOS	68	86
6	Neoplasm, NOS	65	48
7	Epithelial Neoplasm, NOS	71	50
8	Epithelial Neoplasm, NOS	63	71
9	Neoplasm, NOS	64	81
10	Epithelial Neoplasm, NOS	49	29

4. MORTALITY VERSUS CURRENT DIOXIN LEVELS

Since the introduction of the dioxin assay into the morbidity component of this study, all health data has been assessed for associations with dioxin [10]. All dioxin assay results are qualified by a report field defined in Table 9.

Table 9

Report Field Definition

Value	Definition
G	Good result
GND	Good result, below limit of detection
GNQ	Good result, below limit of quantitation
NR	No result

Dioxin assays were administered to all participants who volunteered for the assay at the 1987 physical examination. Table 10 shows a cross classification of all 1261 Ranch Hands by survival status (dead, alive), assay status (yes, no) and report.

Table 10

Ranch Hand Dioxin Assay Status versus Survival

Dioxin assay	Report	Survival Status Alive	Dead	Total
No		242	87	329
Yes	G	848	15	863
	GND	8	1	9
	GNQ	18	2	20
	NR	39	1	40
Total		1155	106	1261

Ranch Hands with missing dioxin results (no assay or assayed with report NR) and nonquantitatable results (report GNQ) were excluded from subsequent analyses of survival versus dioxin. After these exclusions, 856 living Ranch Hands and 16 dead Ranch Hands had dioxin results. Dioxin results are lognormally distributed, hence the logarithm of dioxin was used in the analysis, with one added to the dioxin before taking the logarithm. Univariate summaries of dioxin, expressed in parts per trillion (ppt), and its logarithm, in log(ppt), are summarized in Table 11.

Table 11

Dioxin Summary

Statistic	Dioxin		Log(dioxin+1)	
	Alive	Dead	Alive	Dead
n	856	16	856	16
Minimum	0	0	0	0
Maximum	617.8	179.4	6.4	5.2
Mean	28.4	27.9	2.8	2.7
Median	12.9	11.4	2.6	2.5
Standard Deviation	47.3	43.4	1.0	1.2

The mean values of log(dioxin+1) do not differ significantly with survival status; mean difference=0.11, 95% CI -0.40, 0.62, $p=0.72$.

Of the 16 deceased Ranch Hands with quantitatable dioxin results, 1 died of digestive disease, 4 died of malignant neoplasms, 8 died of circulatory diseases, 1 died of respiratory disease, 1 died of an accident and 1 committed suicide.

An accelerated failure time model for right-censored survival data was fit to assess the relationship, if any, between survival time and the logarithm of dioxin level in Ranch Hands. In this analysis, the survival time of dead Ranch Hands is the time, in years, between the beginning of their tour in Vietnam and death. The survival time of living Ranch Hands is the time, in years, between 31 December 1991 and the beginning of their tour of duty in Vietnam. The analysis was unadjusted, due to the small number (16) of dead Ranch Hands with dioxin values. The dependent variable was the logarithm of survival time and the independent

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variable was log(dioxin+1). The results are summarized in Table
12. There is no significant association between dioxin level and
survival time among Ranch Hands (p=0.99).

Table 12

Survival Time versus Dioxin in Ranch Hands

Coefficient	Chi-square	Degrees of Freedom	95% CI	P-value
0.0004	0.0002	1	-0.06, 0.06	0.99

5. CONCLUSIONS

An evaluation of cumulative all-cause Ranch Hand mortality through 31 December 1991 revealed no statistically significant differences between the observed and expected number of deaths (SMR=1.03, 95% CI 0.85-1.24). The indirectly standardized all-cause Ranch Hand death rate is 3.25 deaths per 1,000 person-years; the Comparison rate is 3.16 deaths per 1,000 person-years. This rate difference is not statistically significant (p=0.75).

Furthermore, the observed number of deaths is not statistically significantly different from the expected number in any of the four subgroups of Ranch Hands determined by rank (officer, enlisted) and job (flyer, nonflyer).

There was a borderline significant increasing trend in the relative risk of death from any cause during the period 1989 through 1991 among flying Ranch Hand enlisted personnel (p=0.06). Of the seven deaths during that period, five were due to malignant neoplasm. Enlisted flyers were, as a group, less exposed to dioxin than enlisted nonflyers. Hence, while this trend is a source of concern, the lack of a corresponding trend among the more heavily exposed enlisted nonflyers suggests that this trend may not be caused by dioxin exposure.

Adjusted cause-specific analyses found no overall significant difference between the observed and expected numbers of deaths for accidental deaths (SMR=1.16), suicides (SMR=0.73), deaths due to malignant neoplasm (SMR=0.85), or deaths due to circulatory diseases (SMR=1.10). However, there is a significant excess of deaths due to circulatory system diseases among nonflying enlisted personnel (SMR=1.57, 95% CI 1.01-2.33, p=0.05). This increase was noted in the last report. The number of such deaths has increased from 19 to 22 and the SMR has decreased from 1.68 to 1.57 since the last report.

There is a significant excess of Ranch Hand deaths caused by diseases of the digestive system (SMR=2.23, 95% CI 1.09-4.10, p=0.03). There was also a significant excess of such deaths among Ranch Hand flying officers (SMR=3.33, 95% CI 1.06-8.03, p=0.04), although the number of deaths in this stratum was small (4). This excess was also noted in the last report and the number of such deaths has remained at nine since then.

There was a significant excess of Ranch Hand deaths due to ill-defined or unknown causes (SMR=6.11, 95% CI 1.02-20.17, p=0.05), although the number of deaths in this stratum was small (2). There was no significant excess of deaths in this category among all Ranch Hands (SMR=2.32, 95% CI 0.59-6.32, p=0.18).

Analysis of survival status versus current dioxin levels found no significant difference between mean dioxin levels among living and dead Ranch Hands among the 872 Ranch Hands with dioxin results. Survival time was also not significantly associated with dioxin levels in Ranch Hands.

In summary, the total all-cause mortality experience of the Ranch Hands is not significantly different from that expected based on the mortality experience of the Comparison population. As of 31 December 1991, 106 (8.4%) of the 1261 Ranch Hands have died; the expected number of deaths is 103. The overall observed and expected numbers of deaths were not significantly different for accidental deaths, suicides and deaths caused by malignant neoplasms and circulatory system diseases. However, significantly increased numbers of Ranch Hand deaths due to digestive diseases and, in nonflying enlisted personnel, circulatory system diseases continue to be seen. Both of these increases have been noted in previous reports and both are, as yet, unexplained.

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PRINCIPAL INVESTIGATORS

William H. Wolfe, MD, MPH, FACPM
Colonel, USAF, MC
Director, Aerospace Medicine

Joel E. Michalek, PhD, GM-15
Senior Research Statistician
Epidemiologic Research Division

Judson C. Miner, DVM, MPH, ACVPM
Colonel, USAF, BSC
Chief Scientist,
Aerospace Medicine Directorate

CONTRIBUTORS

Mr Thomas White
Senior Subject Matter Specialist
QuesTech, Incorporated

Mr Vincent Elequin
Medical Records Administrator
Population Research Branch

Advisory Committee on Special Studies
Relating to the Possible Long-Term Health Effects
of Phenoxy Herbicides and Contaminants:

Earl P. Benditt, MD, University of Washington School of Medicine

Turner Camp, MD, Veterans of Foreign Wars

Captain Ronald F. Coene, USN, National Center for Toxicological Research

Elissa A. Favata, MD, Asst Prof, Robert Wood Johnson Medical School

Michael Gough, PhD, Office of Technology Assessment, Congress of the United States

Robert Harrison, MD, Director of Division of Endocrinology, University of Rochester

Leonard T. Kurland, MD, Mayo Clinic and Mayo Foundation

Peter C. O'Brien, PhD, Mayo Clinic and Mayo Graduate School

Dolores C. Shockley, PhD, Meharry Medical College

Paul D. Stolley, MD, University of Maryland School of Medicine

John F. Young, PhD, National Center for Toxicological Research