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**NON-HODGKIN'S LYMPHOMA IN THE
VIETNAM VETERANS MORTALITY STUDY**

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INTRODUCTION

This paper describes the findings related to non-Hodgkin's lymphoma(NHL) in the Vietnam Veteran Mortality Study conducted by the Veterans Administration. This study was undertaken in response to concerns that elements of the veterans' experience, including herbicide exposure, may make the Vietnam veteran group more susceptible to various diseases.

This proportionate mortality analysis is of deaths found in the Veterans Administration Beneficiary Identification and Records Locator Subsystem(BIRLS). This system includes all veterans whose beneficiaries receive a death benefit. This file contains a relatively complete roster of veterans' deaths. The Office of Environmental Epidemiology requested an ascertainment of mortality in the United States Vietnam era veteran population by the National Academy of Science. Results of this study showed 97.6 percent of deaths among veterans who served in Vietnam were recorded in BIRLS and 82.5 percent of the other Vietnam era veterans' deaths were shown in BIRLS. Of those not serving in Vietnam the distribution of causes of death is not different between the 82.5 percent present and the 17.5 percent not found in BIRLS for cancer or other causes. See Appendix for distribution of causes of death.

METHODS

Study Population

Proceeding under the assumption that the BIRLS system had the potential for yielding a reasonably complete roster of deceased Vietnam era veterans, it was necessary to devise strategies to select these deaths from among all deaths recorded in BIRLS. The selection process was done in several stages. First, it was necessary to obtain as complete a list as possible of all veterans who were likely to have served during the Vietnam era. To do this, all veterans whose service dates included the period 1964-1975 were selected. In addition, for those records where the service dates were missing, veterans whose birthdates were given as falling between 1935 and 1957 inclusive were selected. This yielded about 815,000 records.

Recalling the purpose of the study, to compare the mortality patterns of men who served in Vietnam with those who did not serve in Vietnam, additional criteria were introduced based on time of service and branch of service.

The Vietnam era as defined by the Veterans Administration, was August 5, 1964 to May 7, 1975. Prior to July 1965 and after January 1973 there were relatively few troops in Vietnam. Thus, if one sampled deaths among those who served before 1965 or after January 1, 1973, there would be relatively few decedents who had

served in Vietnam. Thus the study population was limited to military personnel who were in the Armed Forces on July 4, 1965 or who entered service after that date but before March 1, 1973.

Data published by the Department of Defense indicate that 81 percent of those who served in Vietnam were in the Army or Marine Corps. For these branches of service, duty in Vietnam meant, in most cases, service "in country". For those in the Air Force or Navy, Vietnam service often is not so clear cut. It may be difficult to determine whether Navy personnel who were considered to have Vietnam service were ever actually "in country" or if Air Force personnel who were in the Vietnam theatre of operations and flew missions over Vietnam or to Vietnam were ever "in country". Hence the study population was limited even further to persons who served in the Army or Marine Corps between the dates given above. Since this was to be a proportional mortality study and deaths related to the operations of war could only occur in those who served in Southeast Asia and not among those who served elsewhere, deaths occurring among personnel on active duty before the end of 1973 were excluded. The target population as defined by these criteria consisted of 186,000 veterans who died between July 4, 1965 and February 1982 when the study was initiated.

In order to achieve adequate statistical power, it was determined that the study should consist of at least 50,000 eligible cases. It was assumed that some of the cases selected from the target population would not meet the criteria for the study. Therefore the sample size was increased to allow for these anticipated losses. Ultimately, 76,517 names of veterans were randomly selected from the target population.

Military records were searched for all these names (Table 1). Records were found for all but 1032(1.4%) of the names selected; 52,283 of the veterans whose records were found were determined to meet the criteria of the study. That is, they had served with the Army or Marine Corps any time between July 4, 1965 and March 1, 1973. For those men who met the criteria of the study, dates, place of service, military occupation; type of discharge and other demographic data were abstracted from their military records.

Cause of death information has been obtained for 51,421 (98.4%) of the 52,283 men who were determined to be eligible for the study (Table 2). The cause of death in all cases was coded by trained nosologists using the International Classification of Disease, 8th edition (ICDA-8).

All data given in this report will be based on the 51,421 veterans for whom both military service data and cause of death information are available.

Abstracted Information

Items of information abstracted from the death certificates

were: age at last birthday, date of death, underlying cause of death, sex, state of death, race, and histology type if cause of death was cancer.

From the military record the following information was obtained: date first in service, date last in service, branch, date of birth, sex, race, military occupation specialty codes (MOSC), education level, and whether served in Southeast Asia or not. For those serving in Southeast Asia additional information was collected: date first in Southeast Asia, date last in Southeast Asia, units served in, and countries served in.

STATISTICAL ANALYSIS

Proportionate mortality ratios, standardized for age (SPMRs) were calculated. Categories of age were: less than 20, 20-24, ..., 60-64 and 65 and over. SPMRs for categories of cancer are presented in this paper. Vietnam era veterans that did not serve in Southeast Asia were the reference population. Of the 51,421 veterans' deaths in this study 24,736 had served in Southeast Asia, 26,685 had not (Table 3). Southeast Asia veterans that did not go to Vietnam were at most 1.8 percent. SPMRs were calculated for the following subgroups: all army, all marines, and white and nonwhite for army and marines. The Mantel-Haenszel chi-square statistic was calculated for each category to indicate whether the deviation from unity was likely to be seen by chance. A more detailed analysis of non-Hodgkin's lymphoma (NHL) for Marine Corps veterans and black Army veterans is presented.

Case control analyses (Miettinen and Wang) were carried out to examine the relationship between mortality from non-Hodgkin's lymphoma and service in Southeast Asia. Controls for this analysis were all cardiovascular deaths (ICDA-8 codes: 390.0-458.9). These were chosen because both in this mortality study and several others (Anderson, et al; Holmes, et al; Kogan and Clapp; and The Surgeon General, USAF) no association was found between Vietnam service and cardiovascular mortality. Also, no biologic hypothesis exists suggesting a relationship between service in Vietnam or synonymously Southeast Asia and cardiovascular mortality. All analyses were standardized by age to control for confounding by age.

The disadvantages of the SPMR are well known. For example, if the overall mortality rate is different in the exposed and non-exposed populations the SPMR will not approximate the standardized mortality ratio (SMR). That is, if the overall mortality rate is less in other Vietnam era veterans then the cause specific SPMRs will be overestimated for the Southeast Asia veterans. Also, the cause specific SPMR is dependent on the relative distribution of other causes of death. For example, if Southeast Asia veterans had a higher mortality rate for accidents than the referent population, then the SPMR for cancer might be abnormally decreased. The case control analysis is not dependent on this second factor. Also, in case control analysis, if the

exposure of interest is not a risk factor for the selected control group the standardized mortality odds ratio (SMOR) is equivalent to the SMR.

Because of the relative homogeneity of several variables (education, type of discharge, and grade) and correlation of others, it was not felt that significant information would be gained from a multivariate analysis.

RESULTS

The SPMRs presented in Table 4 reveal that only those for lung cancer and non-Hodgkin's lymphoma in Marines are significantly greater than 1 using the Mantel-Haenszel chi-square statistic. The results in the following Tables refer only to NHL, detailed analysis of lung cancer deaths in the Marine Corps will be presented in a separate paper. Nineteen of twenty-four non-white Southeast Asia veterans whose race was not white veterans with NHL were black Army veterans, 3 were in the Marine Corps, and 2 were Army Southeast Asia veterans with race unknown. The SPMR of 1.53 for nonwhite Southeast Asia veterans has a chi-square statistic of 2.30 and corresponding p-value of 0.14. Because the majority are black Army veterans and despite the lack of statistical significance for the nonwhite category, parallel analyses of NHL were done for the subgroup, black Army veterans, as well as for the Marine Corps. The black Marines are included in the Marine analysis. Those with unknown race were excluded from further analysis.

The comparison group for the MORs and SMORs in Tables 5-7f are all cardiovascular deaths. Table 5 presents the age distribution of NHL deaths in these two subgroups. In Table 6 age specific MORs are presented. Marines age 30 through 39 at death have a mortality odds ratio of 5.07 and lower 95% level of 1.49. An overall SMOR, 2.05, standardized for age is presented in Table 7a. The lower 95 percent confidence level is 1.81.

Tables 7b-7g present SMORs for various categories of data collected for these individuals. Grade in service, education level and type of discharge are not presented because of lack of variation of these variables. Ninety-seven percent of the individuals of Table 5 were enlisted personnel, 96 percent were honorable discharges, and more than three quarters had a high school education with other education levels sparsely distributed. Because the values for the categories in Tables 7d and 7e are only present for Southeast Asia veterans all other Vietnam era veterans served as the comparison group for each category. In Tables 7b, 7c, and 7f all veterans have recorded data for the categories therefore the comparison group is all other Vietnam era veterans for that specific category. In Table 7g each ICDA-8 code was compared to all cardiovascular deaths.

Military Occupation Specialty Codes (MOSCs) were categorized as combat troops, direct support of combat troops, and indirect

MOSCs (Table 7c) had the highest SMOR for military occupations at 6.23. A description of the categories of MOSC appear in the Appendix.

Our data base included the dates a veteran first and last served in Southeast Asia. If the difference between these two dates was greater than 13 months there is a significant likelihood this veteran went to Southeast Asia more than once, therefore this analysis is presented as a potential proxy for more than one tour in Southeast Asia. Table 7e presents SMORs by the first year the veteran was in Southeast Asia. Because of the different volumes and contamination of herbicides used during the Vietnam conflict, veterans deaths were categorized by year of first Southeast Asia service. The overwhelming majority of herbicides were applied in 1967 through 1969. Southeast Asia veterans first going to Southeast Asia these years had the highest SMORs.

Table 7f is a categorization of the interval between first going in the military and final discharge. Some veterans may have had 2 or more non-contiguous enlistments. Because this is relatively rare the greater than 4 years category may represent veterans that made the military a 'career'. These individuals serving more than 4 years did not have an increased SMOR.

Table 7g presents SMORs by ICDA-8 coding. The Marine Corps SMOR for ICDA-8 code 200 is elevated. This code includes reticulum-cell sarcoma and lymphosarcoma. In contrast, black Army veterans have a SMOR of 3.82 for ICDA-8 code 202 (giant follicular lymphoma, mycosis fungoides, and other lymphomas).

DISCUSSION

Numerous studies have revealed an association between herbicide use and NHL. A recent population based case control study (Hoar, et al) presented an odds ratio of 2.2 (CI 1.2-4.1) for farmers ever using phenoxyacetic acids. A matched case control study (Hardell, et al) of malignant lymphomas (Hodgkin's disease and NHL) showed a calculated relative risk of 4.8 for exposure to phenoxy acids. In that study persons with concomittant high-grade exposure to chlorophenols were excluded. Because Agent Orange and other herbicides used in Vietnam contain phenoxyacetic acids, it is essential to attempt to associate a level of exposure to one or more of these agents to a particular individual. Future efforts of the Office of Environmental Epidemiology include associating location of a Southeast Asia veteran's unit with known spraying missions. Also, an additional sample of veterans' deaths from 1982-1984 is being prepared. From this further data we hope to see if disproportionate deaths from NHL continues to occur among veterans with Southeast Asia exposure.

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APPENDIX

1. The following is a description of the Military Occupation Service Codes. The exact codes used are identical to those used in the Wisconsin Vietnam Veteran Mortality Study (Anderson, et al).

Combat. Occupations with primary duty involving direct offensive and defensive actions against an armed hostile enemy force. For example: rifleman, assaultman, field artillery batteryman, or mortar man.

Direct. Occupations with primary duty involving support of combat troops that may involve limited direct and/or extensive indirect contact with an armed hostile force. For example: electrical systems technician, bulk fuel specialist, wireman or field radio operator.

Indirect. Occupations with primary duty involving indirect support of combat and/or direct support troops that does not involve contact with an armed hostile force. For example: cook, aircraft ballistics computer technician, radar repairman, and clerk.

2. The following are ICDA-8 codes associated with the categorization of cancer mortality in Table 4.

Category	ICDA-8 Code
Other causes	0-136, 210-228, 240-989
Buccal	140-149
Esophagus	150
Stomach	151
Intestines, etc.	152-154, 158, 159
Liver, biliary	155-156
Pancreas	157
Upper resp.	160-161
Lung	162
Bone	170
Soft tissue	171
Melanoma	172
Prostate	185
Testis	186
Bladder	188
Kidney	189
Brain	191
Other nervous system	192
Thyroid and endocrine	193-194
Non-Hodgkin's lymphoma	200, 202
Hodgkin's	201
Multiple Myeloma	203
Leukemia	204-207
Other cancer	163, 173-174, 187, 190, 195- 199, 208-209, 230-239

3. The following is the distribution of causes of death from the National Academy of Sciences Ascertainment of Mortality in the U. S. Vietnam Veteran Population for all veterans not going to Vietnam. Forty-five percent of these veterans were Vietnam era veterans. The 'other' category includes cardiovascular disease.

Cause	Found in BIRLS No. (%)	Not Found in Birls No. (%)
Cancer	97 (9.7)	23 (9.6)
Other	231 (23.0)	58 (24.2)
Motor Vehicle	237 (23.6)	52 (21.7)
Suicide	163 (16.2)	25 (10.4)
Homocide	123 (12.2)	38 (15.8)
Other Trauma	42 (4.2)	13 (5.4)
Unknown	112 (11.1)	31 (12.9)
Total	1005 (100.0)	240 (100.0)

TABLE 1: The Study Sample--Military Records Search.

	Number	Percent
All names selected	75617	100.0%
Records not found	1032	1.4%
Records found, ineligible	22302	29.5%
Records found, eligible	52283	69.1%

Ineligibility was based on: a. wrong branch of service, b. wrong time of service

Table 2: Results of Death Certificate Search.

	Number	Percent
Eligible cases	52283	100.0%
No cause of death	862	1.6%
Coded cause of death	51421	98.4%

Table 3: Distribution of Eligible Deaths by Branch of Service, Race, and Place of Service.

	Army		Marines	
	Southeast Asia	Other Service	Southeast Asia	Other Service
White	15734	18215	3943	3120
Nonwhite ¹	4399	4689	760	661
	20133	22904	4603	3781

¹ Nonwhite includes unknown race.

Table 4: Standardized Proportionate Mortality Ratios (SPMRs) by Branch of Service and Race.

¹ SPMR	Army	Marines	White	Nonwhite ²
Other causes	1.00	0.98	1.00	0.99
Buccal	0.92	2.21	1.09	0.85
Esophagus	1.29	0.39	0.90	1.72
Stomach	1.13	0.81	0.99	1.33
Intestines, etc.	0.97	1.25	1.05	0.82
Liver, biliary	1.01	1.20	1.28	0.69
Pancreas	0.88	1.62	0.98	0.82
Upper resp.	1.19	0.18	0.99	1.13
Lung	1.03	1.57*	1.09	1.11
Bone	0.86	1.35	1.03	0.59
Soft tissue	1.03	0.70	0.93	1.06
Melanoma	1.04	0.93	0.99	3.33
Prostate	0.89	1.29	0.68	3.16
Testis	1.11	1.26	1.20	0.60
Bladder	0.61	2.39	0.90	0.28
Kidney	0.89	0.95	0.83	1.56
Brain	0.96	1.05	0.99	0.85
Other nervous	0.55*	0.92	0.62*	0.43
Thyroid, endo.	0.58	0.56	0.58	0.57
Non-Hodgkin's	0.82	2.08*	0.89	1.53
Hodgkin's	1.15	1.37	1.22	1.01
Multiple Myeloma	0.80	0.45	0.68	1.21
Leukemia	0.88	1.12	0.89	1.14
Other cancer	1.03	1.06	1.00	1.23

* p-value for Mantel-Haenszel chi-square 1 degree of freedom < .05.

1 See Appendix from respective ICDA-8 codes.

2 Nonwhite includes unknown race.

Table 5: Age Distribution of Non-Hodgkin's Lymphoma.

	Marines		Black Army	
	SE Asia Service	Non SE Asia Service	SE Asia Service	Non SE Asia Service
20-29	7	4	4	3
30-39	23	3	13	4
40-49	2	2	2	1
50-59	2	1	0	1
60+	1	0	0	0
Total	35	10	19	10

Table 6: Age Specific Mortality Odds Ratios for Non-Hodgkin's Lymphoma.¹

	Marines	Black Army
	MOR (LCI, UCI)	MOR (LCI, UCI)
20-29	2.17 (0.60, 7.75)	3.15 (0.67, 14.8)
30-39	5.07 (1.49, 17.2) *	2.86 (0.92, 8.86)
40-49	0.28 (0.04, 2.02)	0.53 (0.07, 3.85)
50-59	0.95 (0.08, 10.7)	--
60+	1.58 (0.05, 48.8) **	--

* p-value for Mantel-Haenszel chi square < .01.

** number of exposed cases is one.

¹ Cardiovascular deaths are the control population.

Table 7a: Overall Standardized Mortality Odds Ratio¹
for Non-Hodgkin's Lymphoma.

	Marines SMOR(LCI,UCI)	Black Army SMOR(LCI,UCI)
	2.05(1.81,2.30)	1.78(0.93,3.42)

1 Cardiovascular deaths are the control population.

Table 7b: Standardized Mortality Odds Ratio for¹
Non-Hodgkin's Lymphoma by Year of Death.

	Marines SMOR(LCI,UCI)	Black Army SMOR(LCI,UCI)
1965-76	2.70(0.80,9.19)	0.58(0.00,280.)
1977-79	1.79(0.51,6.21)	1.79(0.64,5.06)
1980-82	2.57(0.94,7.06)	2.90(0.76,11.0)

1 Cardiovascular deaths are the control population.

Table 7c: Standardized Mortality Odds Ratio for¹
Non-Hodgkin's Lymphoma by Military Oc-
cupation Specialty Code(MOSC).

	Marines SMOR(LCI,UCI)	Black Army SMOR(LCI,UCI)
Combat	6.23(1.28,30.2)	2.20(0.58,8.38)
Direct	0.72(----,----) ²	1.35(0.58,3.15)
Indirect	2.31(0.39,13.9)	1.95(0.57,6.73)

1 Cardiovascular deaths are the control population.

2 Confidence interval not calculated.

1

Table 7d: Standardized Mortality Odds Ratio for Non-Hodgkin's Lymphoma by Potential Tours of Service in Southeast Asia.

	Marines SMOR (LCI, UCI)	Black Army SMOR (LCI, UCI)
LE 13 MO	2.39 (1.26, 4.53)	1.73 (0.79, 3.80)
GT 13 MO	1.23 (0.78, 1.93)	1.92 (0.91, 4.05)

1 Cardiovascular deaths are the control population.

1

Table 7e: Standardized Mortality Odds Ratio for Non-Hodgkin's Lymphoma by First Year in Southeast Asia.

	Marines SMOR (LCI, UCI)	Black Army SMOR (LCI, UCI)
1965-66	1.76 (1.02, 3.03)	1.89 (0.72, 4.95)
1967-69	2.51 (1.22, 5.21)	1.96 (0.94, 4.10)
1970+	1.68 (0.39, 7.18)	0.73 (0.11, 4.81)

* Number of exposed cases is one.

1 Cardiovascular deaths are the control population.

1

Table 7f: Standardized Mortality Odds Ratio for Non-Hodgkin's Lymphoma by Potential Years in Military Service.

	Marines SMOR (LCI, UCI)	Black Army SMOR (LCI, UCI)
LE 4 YRS	3.61 (1.49, 8.73)	2.93 (1.29, 6.66)
GT 4 YRS	0.85 (----, ----) ²	0.55 (0.12, 2.57)

1 Cardiovascular deaths are the control population.

2 Confidence interval not calculated.

1

Table 7g: Standardized Mortality Odds Ratio for
Non-Hodgkin's Lymphoma by ICDA-8 Code.

	Marines SMOR (LCI, UCI)	Black Army SMOR (LCI, UCI)
Code=200	2.33(1.12, 4.85)	1.12(0.65, 1.92)
Code=202	1.85(0.82, 4.18)	3.82(1.15, 12.7)

1 Cardiovascular deaths are the control population.