

PROJECT RANCH HAND II

**AN EPIDEMIOLOGIC INVESTIGATION OF HEALTH
EFFECTS IN AIR FORCE PERSONNEL FOLLOWING
EXPOSURE TO HERBICIDES**

BASELINE MORTALITY STUDY RESULTS

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The purpose of this report is to present the baseline mortality study results. As of December 31, 1982, 50 Ranch Hand and 250 comparison subjects had died (certified on/before April 27, 1983). Data analysis showed that the mortality experience of the Ranch Hand group is nearly identical to that of this comparison group. However, this mortality report can in no way be regarded as conclusively negative since the study population may not yet have reached the latency period. Subsequent mortality reports will include additional analyses and will be updated annually for the next 20 years.

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EXECUTIVE SUMMARY
Baseline Mortality Study

The Ranch Hand II epidemiologic study uses a matched cohort design in a nonconcurrent prospective setting, incorporating mortality, morbidity, and follow-up studies. The purpose of this report is to present the baseline mortality study results.

Since 1979, a detailed population ascertainment process has enumerated a total of 1269 Ranch Hand personnel who served in Vietnam during the period of 1962-1971. As described in the protocol, this total is believed to comprise the entire exposed study population. The eligibility of each Ranch Hander was verified by a hand review of his personnel record. A comparison group was formed by identifying all individuals assigned to selected Air Force organizational units with a mission of flying cargo to, from, and in Vietnam during the same period. All Ranch Hand and comparison subjects designated as killed in action were removed from the study population. By a computerized nearest neighbor selection process, up to 10 comparison individuals were matched to each Ranch Hander by job category, race, and age to the closest month of birth. A hand record review of the matched comparison sets revealed that on the average, 8.2 comparison individuals were fully suitable for study. From each matched comparison set, five individuals were randomly selected for the mortality study, yielding a 1:5 design. Every Ranch Hander and his set of comparisons will be the subjects of annual mortality updates throughout the entire 20 years of the follow-up study so that emerging mortality patterns or disease clusters may be detected with maximal sensitivity. Each living Ranch Hander and his first and willing comparison match were selected to participate in a comprehensive physical examination and an in-home interview; the results of this study will be presented in a subsequent report in late 1983.

A mortality determination on 1,247 Ranch Handers and 6,171 comparison subjects was made, sequentially using the data sources of the Air Force, Veterans Administration, Social Security Administration, Internal Revenue Service, and personal contact efforts. As of December 31, 1982, 50 Ranch Hand and 250 comparison subjects had died (certified on/before April 27, 1983). Death certificates were obtained on all 300 deceased subjects and were coded by an Air Force nosologist (ICD, 9th ED). All codings were verified by the National Center for Health Statistics. Autopsy results are currently being sought for future analyses.

Statistical analyses of noncause specific death emphasized survival curve estimates, linear rank procedures, relative risk estimates, and standardized mortality ratios (SMRs). Cause specific analyses were limited to relative risk estimates because of small cell sizes. In addition to these approaches, three other data bases were contrasted to the Ranch Hand population, where possible; the 1978 US White Male Mortality experience, the 1978 Department of Defense (DoD) Nondisability Retired Life Table, and the mortality experience of the West Point Class of 1956. These additional comparison groups have substantial comparability or sample size limitations, rendering conclusions to the weakest order. Analyses with these "external" comparison groups were accomplished to crudely define the healthy worker effect and to determine if the Ranch Hand group mortality was drastically out of line with that of other military populations.

Data analysis showed that the mortality experience of the Ranch Hand group is nearly identical to that of the comparison group. Analyses showed that officers are living longer than enlisted personnel in both Ranch Hand and comparison groups. This difference between officers and enlisted personnel was statistically significant in the comparison group whereas it was not in the Ranch Hand cohort. A contrast of the Ranch Hand and comparison group to the 1978 DoD Life Table showed significantly less mortality for Ranch Hand officers, comparison officers and comparison enlisted men, however, there was not a statistically significant favorable mortality rate for Ranch Hand enlisted personnel. This pattern of mortality was also seen in a contrast of the Ranch Hand and comparison groups to the 1978 U.S. white male mortality experience. That is, highly favorable mortality differentials for Ranch Hand officers, comparison officers and comparison enlisted personnel were observed, but not for Ranch Hand enlisted. This trend is consistent with the self perceptions of differential herbicide exposures reported by many of the Ranch Hand subjects. The reason(s) for these observations are speculative at present, but may include the related items of sample size, socioeconomic differences, access to medical care, and health education and possible herbicide effects. Cause specific analyses were statistically nonsignificant. The Ranch Handers showed a relative paucity of overall cancer but an excess of digestive disorder deaths, both statistically nonsignificant. No soft tissue sarcoma deaths were detected in either group. Analyses of both the Ranch Hand and the comparison groups to the 1978 US White male mortality experience showed highly significant favorable findings. Most of these differences are speculatively attributed to the healthy worker effect. A contrast of the Ranch Hand and comparison groups to the 1978 DoD Life Table showed significantly less mortality for Ranch Hand officers and comparison officers and enlisted men. The West Point comparison showed nonsignificant SMRs of 0.530 and 0.778 for the Ranch Hand officers and the comparison group officers, respectively. Overall, the limitations of the statistical power calculations in most of these analyses were substantial in most analyses due to 1) the low mortality rate (4%) in the Ranch Hand and comparison groups to date, 2) the inherently small group of Ranch Handers (as described in the study protocol), and 3) the observed relative risks which approached unity in most categories.

This baseline mortality report can in no way be regarded as conclusively negative because this small, young, and relatively healthy cohort may not have yet reached the latency period wherein attributable fatal disease might be expected and detected within limited power boundaries of this study. Future commitments for the annual mortality updates include detailed covariate analyses for disease risk factors, herbicide exposure, and confounding industrial chemical exposures. Further, subsequent morbidity reports will include full spectrum, disease specific analyses, e.g., cancer (fatal, ongoing, cured) in an effort to enhance study sensitivity to emerging herbicide effects, if they occur.

PREFACE

In October 1978, the United States Air Force (USAF) Surgeon General made the commitment to the Congress and to the White House to conduct an epidemiologic study of the possible adverse health effects arising from the herbicide exposure of Air Force personnel who conducted aerial dissemination missions in Vietnam (Operation Ranch Hand). The purpose of this epidemiologic investigation is to determine whether long-term adverse health effects exist and whether they can be attributed to occupational exposure to herbicides and their contaminants. The study protocol (1) for this effort incorporates a matched cohort design placed in a nonconcurrent prospective setting. The study approach includes mortality, morbidity, and follow-up elements linked tightly in time, in order to produce the most data in the shortest period of time. The study addresses the question: Has there been, or are there currently, or will there be any adverse health effects among former Ranch Hand personnel caused by repeated occupational exposure to 2,4,5-T containing herbicides and the contaminant, TCDD? At the request of the Principal Investigators (see Appendix I) the study protocol was extensively and independently peer reviewed. The review agencies included: The University of Texas School of Public Health, Houston Texas; the USAF Scientific Advisory Board; the Armed Forces Epidemiological Board; and the National Research Council of the National Academy of Sciences. In 1980, the Science Panel of the Agent Orange Working Group was created as an additional peer review agency. This group, redesignated as the Advisory Committee on Special Studies Relating to the Possible Long-Term Health Effects of Phenoxy Herbicides and Contaminants, has consented to the oversight responsibility of the Ranch Hand study and continues to monitor the conduct of this epidemiologic investigation (see Appendix II). The approved and official protocol for this effort is available to the public through the National Technical Information Services, 5285 Port Royal Road, Springfield, Virginia 22161.

The Ranch Hand II Study protocol heralds the suboptimal statistical power of the mortality study. The mortality study was motivated by the desire to use a full spectrum epidemiologic approach to the herbicide question. Additionally, the investigators were scientifically obliged to pursue the mortality study because of previous and emerging studies (some with small sample sizes) which suggested the possibility of a soft tissue sarcoma end point (2,3,4). Within the inherent sample size limitation of the Ranch Hand population, detection of such a rare condition will be missed unless there is marked case clustering and correspondingly high relative risks.

Also, because of sample size limitations as well as the myriad of proposed clinical end points, a case-control design was not entertained. The investigators have attempted to enhance statistical power and analytic sensitivity where possible by using 1) a large comparison group, 2) precise matching procedures, 3) annual mortality updates, 4) mortality-morbidity linkages, 5) a lengthy follow-up study, 6) external comparison groups, and 7) state-of-the-art statistical methodology. A final assessment of overall mortality must necessarily await substantially more data and covariate approaches to identify and isolate unusual emerging mortality patterns, if they occur.

This report is primarily directed to individuals with statistical and epidemiologic backgrounds. It also assumes that the reader has a familiarity with the herbicide/dioxin issue and a detailed knowledge of the protocol of the Air Force study. In the interest of brevity, the reader is referred to the protocol published as US Air Force School of Aerospace Medicine Technical Report 82-44.

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