Epidemiology Studies of Vietnam Veterans: A Critical Review

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Introduction

A number of epidemiologic studies of Vietnam veterans have been conducted to evaluate whether there is a causal relationship between exposure to Agent Orange and human health effects. In addition to the extensive studies of the members of Operation Ranch Hand and the U.S. Army Chemical Corps, other veteran groups have been examined including Australian National Servicemen, Korean Vietnam Veterans, and several studies of Vietnam veterans conducted by the Centers for Disease Control (CDC) and the Department of Veterans Affairs (DVA). These studies have provided considerable data on the health status of veterans.

Materials and Methods

All of the epidemiologic studies are observational and therefore, warrant careful attention with respect to bias and confounding. In addition to summarizing the major studies of Vietnam veterans, the studies will be evaluated on: (1) selection of participants; (2) quality of exposure data; (3) methods of outcome ascertainment; (4) appropriateness of statistical analyses; and (5) validity of the authors' conclusions

Results and Discussion

The Vietnam Veterans' Association of Australia (VVAA), established in 1979, has claimed that Australian Vietnam veterans were heavily exposed to TCDD during the conflict and as a result, are at increased risk for deaths due to cancer. In order to evaluate these claims, a Royal Commission on 'The Use and Effects of Chemical Agents on Australian Personnel in Vietnam' was appointed in 1983. Based primarily on US records of herbicide use, the Commission concluded that few Australian Vietnam veterans were exposed to TCDD. [1] During their evaluation of the epidemiologic data, the Commission relied on the studies of Ranch Hand veterans as well as the cohort mortality study of Australian National Servicemen, which found no significant increase in risk of death due to cancer but did find increase risk due to other causes unrelated to TCDD exposure (e.g., alcohol related diseases, accidents).[2, 3] Additional studies of Australian Vietnam veterans include a case-control study, which examined the potential association between Vietnam service and risk of congenital abnormalities. [4] No evidence was found that service in Vietnam increased the risk of fathering children with these abnormalities compared to non-veterans. With use of Agent Orange varying over the entire Vietnam conflict, military phase and location could serve as an indirect measure of exposure. In a cohort study of veterans for both military phase and service location there were no differences in veteran mortality.[5]

The Department of Veterans Affairs has conducted several mortality studies including one of female Vietnam veterans. [6] This study, an update of a 1991 study, examined mortality rates of women serving both in Vietnam and outside Vietnam compared to US women. A non-significant risk of death among female Vietnam veterans compared to women serving outside of Vietnam was observed (RR=2.8; 95% CI: 0.8-10.2), primarily due to an elevated risk observed among Vietnam veteran nurses. Other studies by the DVA included studies of US Marine veterans that served in

Vietnam.[7] Excessive deaths due to malignant melanomas including Hodgkin's disease (HD) and non-Hodgkin's lymphoma (NHL) associated with dioxin exposure were reported. However, the small number of non-Vietnam veterans' deaths used as a comparison group in this study and incomparable age distributions of the two groups greatly affected the PMRs, particularly for rare cancers such as HD and NHL. The DVA also conducted hospital-based case-control studies of HD and NHL.[8] These studies found that Vietnam service was not associated with increased risk of mortality due to NHL nor was it associated with a significant increase in the risk of HD (adjusted OR = 1.28; 95% CI = 0.94-1.76).

In 1987, the Centers for Disease Control released mortality results from the Vietnam Experience Study, a random sample of enlisted US Army veterans from 1965-1971.[9] They reported a 17% higher rate of mortality among Vietnam veterans compared to veterans serving in the US, Korea, or Germany. However, this difference is observed during the first five years after discharge. With subsequent years of follow-up, the difference in mortality between Vietnam and non-Vietnam veterans disappeared. The 1990 Selected Cancers Study was a population-based, case-control study, which further evaluated possible associations between Vietnam service and cancer outcomes.[10] The CDC's findings suggested an increased risk of non-Hodgkin's lymphoma among Vietnam veterans. However, they did not find any evidence that this increased risk was related to Agent Orange exposure. Veterans who served in III Corps, the region with the greatest Agent Orange use, had a lower risk of NHL than veterans who served in other regions.

In the studies of Korean veterans, over 4,000 people from the Korean government registry of Vietnam veteran "Agent Orange victims" and a reference population consisting of non-Vietnam veterans and veterans that were deployed to Vietnam but were considered unexposed to herbicides were invited to participate in a clinical evaluation which included an interview, a physical examination, an eye examination, and routine testing such as urinalysis, blood count, fasting blood sugar, and a pulmonary function test.[11-13] Exposure assessment was based on self-reports and area exposure estimates.

There were 88 various outcomes identified among the study participants. Some included conventional diagnoses such as lung cancer, liver cirrhosis, and Parkinson's disease, while others represented non-specific syndromes such as "vasculopathy," "amnestic disorder"[sic], or "motor neuron disease." Some outcomes such as "macrocytosis" or "uroporphyrin" were non-specific laboratory findings. The criteria for considering such findings abnormal and their clinical significance were not reported.

There were a number of statistically significant findings reported. However, there are several concerns regarding the Korean veterans' study. Probably most important is the method for selection of study participants. The "exposed" group was selected among "Agent Orange victims," i.e., Vietnam War veterans that claimed both exposure to Agent Orange and disease associated with it. The level of effort to recruit study participants was different for the exposed and the unexposed. Moreover, the "exposed" non-respondents were contacted by phone and received a second mail survey. No such effort was made to recruit the unexposed controls. Thus, the overall participation rate was 34.7% among "Agent Orange victims," 5.6% among unexposed Vietnam controls, and 0.6% among non-Vietnam controls.

A higher proportion of persons in the exposed group compared to controls underwent specialized evaluations. For example, 78% of the exposed saw a neurologist compared to 28% of controls.

Therefore, certain conditions may have been more likely to be diagnosed among the exposed than among the unexposed.

1. The interpretation of the study results will also be examined. The authors reported that 12 outcomes showed "strong connections with the level of herbicides." However, a closer examination of the underlying information shows several instances where the data may have been misinterpreted. For example, the re-analysis for psoriasis showed a statistically significant increased risk for those exposed only when compared to non-Vietnam controls and only in the lowest exposure group. There was a negative association when compared to non-exposed Vietnam veterans.

The specific methodological issues will be assessed in terms of their impact on the results of the specific studies and on the overall interpretation of the major studies of Vietnam veterans.

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